(19) Eur päisches Patentamt
Eur pean Pat nt Offic
Office européen des brevets

(11) Publication number: **0 516 069 A1**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **92108916.5**

(22) Date of filing: **27.05.92**

(51) Int. Cl.5: **C07D 213/81**, C07D 277/46, C07D 401/06, C07D 401/12, C07D 401/14, C07D 417/12, C07D 417/14, C07D 241/24, C07C 233/82, A61K 31/44, A61K 31/425

(30) Priority: **31.05.91 JP 157725/91**

(43) Date of publication of application: **02.12.92 Bulletin 92/49**

(84) Designated Contracting States: **AT BE CH DE DK ES FR GB GR IT LI NL PT SE**

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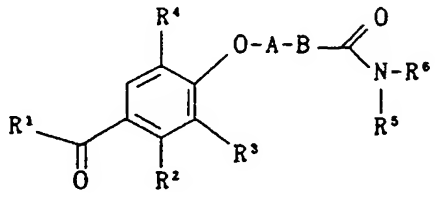
(54) Leukotriene B4 antagonist.

(57) Leukotriene B_4 antagonists of the formula:



wherein each symbol is as defined in the specification, processes for producing them, and pharmaceutical compositions containing them. The compounds of the present invention are very useful as the drugs for the treatment of allergic and inflammatory diseases.

EP 0 516 069 A1

BACKGROUND OF THE INVENTION

TECHNICAL FIELD

The present invention relates to compounds effective as leukotriene B_4 antagonists.

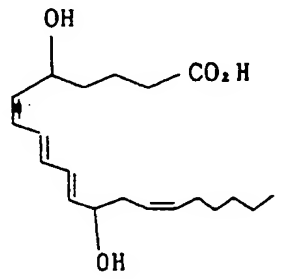
More particularly, this invention relates to leukotriene B_4 antagonists, to processes for producing them and to pharmaceutical compositions containing at least one of those leukotriene B_4 antagonists, which have excellent anti-leukotriene B_4 activity and are useful as an anti-allergic agent or an anti-inflammatory agent.

PRIOR ART

In 1979 B. Sammuelsson reported the isolation and biological effects of leukotrienes (B. Sammuelsson et al. (1980): Advances in Prostaglandin and Thromboxane Research, Vol. 6, edited by B. Sammuelsson, R. Ramwell, and R. Paaletti, P. I. Raven Press, New York).

Since then, a tremendous amount of research in the synthetic organic chemistry and pharmacology of leukotriene A_4, B_4, C_4, D_4, etc. has been performed.

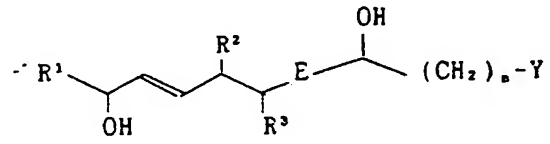
Leukotrienes induce an increase in capillary permeability and cause smooth muscle contraction. Leukotriene B_4, one of leukotrienes which is shown below, has different pharmacological properties from the others. It is chemotactic for macrophages and neutrophils at concentrations of ~ 1 ng/ml (greater than any other known lipid chemotactic factor). It is detected in the synovia of patients with rheumatoid arthritis or gouty arthritis, and in the sputum of obstructive airways diseases which suggest that it is a primary mediator of inflammatory and allergic states.



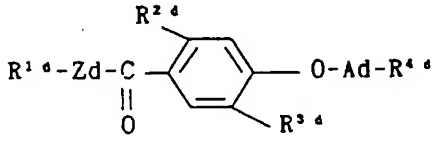
Leukotriene B_4

In recent research some compounds having an antagonism on LTB_4 have been reported. For example,

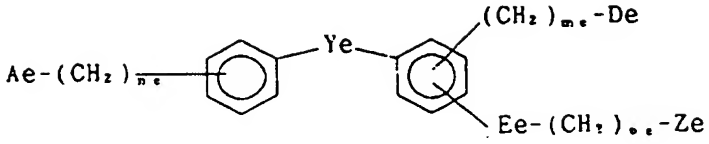
1) EP-A-0183177 (SUMITOMO PHARMACEUTICALS CO.)



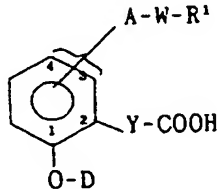
2) EP-A-276065 (ELI LILLY & CO)



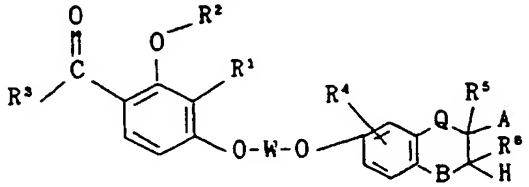
3) EP-A-276064 (ELI LILLY & CO)



4) EP-A-0405116 (ONO PHARMACEUTICAL CO)



5) EP-A-292977 (SEARLE G D & CO)



6) WO-A-8805045 (UPJOHN CO)

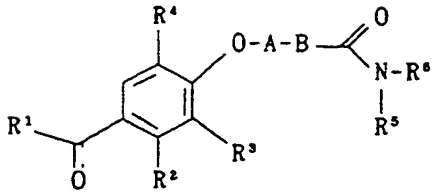
B-C-C≅CH$_2$C(M$_2$)-C≅C-Y-C(M$_1$)-A
B-C-C≅CH$_2$C(M$_2$)-C≅C-P-R$_5$-A

SUMMARY OF THE INVENTION

In accordance with the present invention, leukotriene B_4 antagonists of the following general formula [I] and their non-toxic pharmaceutically acceptable salts are provided, which have potent anti-leukotriene B_4 activity which include suppression of chemotaxis, degranulation and O_2-production of leukocytes, and modulation of lymphocytes activity, etc. This action may render these compounds very useful as the drugs for the treatment of inflammatory states or immunological disorders such as allergy, rheumatoid arthritis, inflammatory bowel disease.

DISCLOSURE OF THE INVENTION

The novel leukotriene B_4 antagonists provided by the present invention are those represented by the formula [I]:



wherein

A is a C_1-C_5 alkylene chain;

B is a phenylene or 6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms, and B may be, optionally substituted with one or two substituents selected from the group, consisting of a C_1-C_5 alkyl group, a C_1-C_5 alkoxy group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

R^1 is a C_1-C_5 alkyl group;

R^2 is a hydroxyl group or a C_1-C_5 alkoxy group;

R^3 and R^4 are each independently a hydrogen atom, a C_1-C_5 alkyl group, a C_2-C_5 alkenyl group or a C_2-C_5 alkynyl group;

R^5 is a hydrogen atom, a C_1-C_5 alkyl group or a hydroxy C_1-C_5 alkyl group;

R^6 is a group of the formula:

$$-X-Y-Z-R^{6'}$$

wherein X is a phenylene group or a monocyclic 5~ 6 membered hetero aromatic group, and X is optionally substituted with one or two substituents selected from the group consisting of a C_1 -C_5 alkyl group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

Y is a single bond or an oxygen atom;

Z is a single bond or a C_1-C_5 alkylene chain;

provided that when Y is an oxygen atom,

X is a phenylene group and Z is a C_1-C_5 alkylene chain;

$R^{6'}$ is a $COOR^7$ group,

a $CONR^8R^9$ group,

a $CONHCHR^{20}(CH_2)_nCOOR^7$ group,

a $CONHCHR^{20}(CH_2)_nCONR^8R^9$ group,

a $CONHCHR^{20}CONHCHR^{22}CO_2R^7$ group or

a sulfamoyl group,

wherein R^7 is a hydrogen atom, a benzyl group, a C_1-C_5 alkyl group or an C_1-C_5 alkyl group substituted with an aminoheteroaromatic group wherein the heteroaromatic group is a monocyclic 5~6 membered heteroaromatic group;

R^8 and R^9 are each independently a hydrogen atom, a C_1-C_5 alkyl group, hydroxy C_1 -C_5 alkyl group, a hydroxyethylpyridyl group or a hydroxyethylthiazolyl group, or the group of the formula:

$$-NR^8R^9$$

represents a pyrrolidino, a piperidino or a morpholino group;

R^{20} is a hydrogen atom, a hydroxyl group, a C_1-C_5 alkyl group, a phenyl group, a hydroxyphenyl group, a benzyl group, a hydroxy benzyl group or a substituted C_1-C_5 alkyl group wherein the substituent is selected from the group consisting of a hydroxyl group, a C_1-C_5 alkoxy group, a mercapto group, a methylthio group, an amino group, an indolyl group, an imidazolyl group, a carboxyl group, a C_1-C_5 alkoxycarbonyl group, a carbamoyl group and a guanidino group;

n is 0, 1, 2, 3, 4 or 5; and

R^{22} is a hydrogen atom, a C_1-C_5 alkyl group or a C_1-C_5 hydroxyalkyl group;

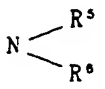
or R^6 is a $CHR^{20}(CH_2)_nCOOR^7$ group,

a $CH_2CHR^{20}COOR^7$ group,

a $CHR^{20}(CH_2)_nCONR^8R^9$ group,

a $CH_2CHR^{20}CONR^8R^9$ group,

a $CHR^{20}(CH_2)_nOH$ group,
a $CR^{20}R^{22}(CH_2)_nOH$ group,
a $CH_2CHR^{20}OH$ group, or
a $CHR^{20}CONHCHR^{22}CO_2R^7$ group,
wherein R^7, R^8, R^9, R^{20}, R^{22} and n are as defined above, or the group of the formula:



represents an azetidino group, pyrrolidino group, a piperidino group or a homopiperidino group, which is optionally substituted with one to two substituents selected from the group consisting of a hydroxyl group, a C_1-C_5 hydroxyalkyl group, carboxyl group, C_1-C_5 alkoxycarbonyl group and benzyloxycarbonyl group; or pharmaceutically acceptable salts thereof.

In the definitions as used above, the term "C_1-C_5 alkylene" means a straight or branched chain C_1-C_5 alkylene (e.g. methylene, ethylene, trimethylene, tetramethylene, pentamethylene, 1-methylethylene, 2-ethyltrimethylene, etc.).

The term "C_1-C_5 alkyl" means a straight or branched chain C_1-C_5 alkyl (e.g. methyl, ethyl, n-propyl, iso-propyl, n-butyl, iso-butyl, sec-butyl, tert-butyl, n-pentyl, iso-pentyl, sec-pentyl, neo-pentyl, etc.).

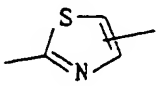
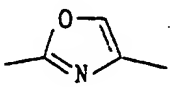
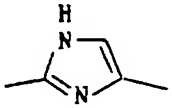
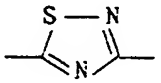
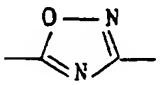
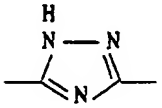
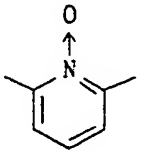
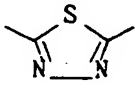
The term "C_2-C_5 alkenyl" means a straight or branched chain C_2-C_5 alkenyl (e.g. 1-methylethenyl, 1-ethylethenyl, 1-propenyl, 2-propenyl, 1-methyl-1-propenyl, 2-methyl-1-propenyl, 1-methyl-2-propenyl, 2-methyl-2-propenyl, 1,2-dimethyl-1-propenyl, 1-n-butenyl, 2-n-butenyl, 3-n-butenyl, 1-methyl-1-butenyl, 2-methyl-1-butenyl,3-methyl-1-butenyl, 1-methyl-2-butenyl, 2-methyl-3-butenyl, 3-methyl-3-butenyl, 1-pentenyl, 2-pentenyl, 3-pentenyl, 4-pentenyl, etc.).

The term "C_2-C_5 alkynyl" means a straight or branched chain C_2-C_5 alkynyl (e.g. ethynyl, 1-propynyl, 2-propynyl, 1-methyl-2-propynyl, 1-n-butynyl, 2-n-butynyl, 3-n-butynyl, 3-methyl-1-butynyl, 1-methyl-2-butynyl, 2-methyl-3-butynyl, 1-pentynyl 2-pentynyl 3-pentynyl, 4-pentynyl, etc.).

The term "C_1-C_5 alkoxy" means alkoxy having C_1-C_5 alkyl moiety (e.g. methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy, n-pentoxy, iso-pentoxy, sec-pentoxy, neo-pentoxy, etc.).

The term "6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms" includes pyridinediyl, pyrazinediyl, pyrimidinediyl, etc.

The term "monocyclic 5~6 membered heteroaromatic group" contains, for example, 1-3 hetero atoms which can be a nitrogen, oxygen or sulfur atom, or an oxydized nitrogen atom (N →O), and examples of the monocyclic 5-6 membered heteroaromatic group are a pyridinediyl group and any one of the group of the formula (i)-(viii):

(i) 
(ii) 
(iii) 
(iv) 
(v) 
(vi) 
(vii) 
(viii) 

The term "hydroxyphenyl group" may be a 2-hydroxyphenyl, a 3-hydroxyphenyl or a 4-hydroxyphenyl group.

The term "hydroxybenzyl group" may be a 2-hydroxybenzyl, a 3-hydroxybenzyl or a 4-hydroxybenzyl group.

The term "halogen" may be a chlorine, a bromine or a fluorine atom.

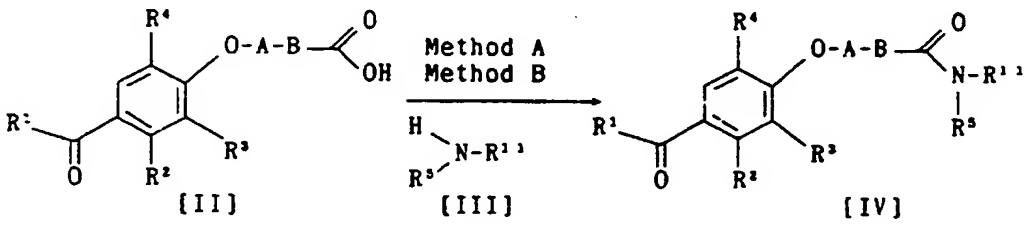
The term "indolyl group" may be a 2-indolyl or 3-indolyl group.

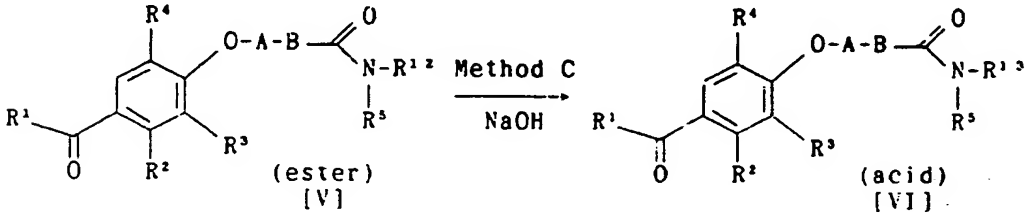
The term "imidazolyl group" may be a 4-imidazolyl group.

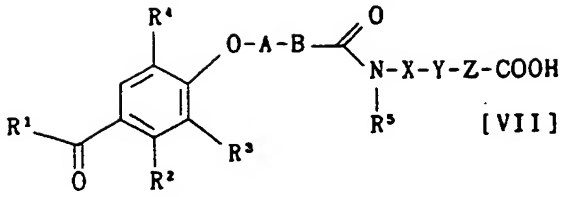
A basic object of the present invention is to provide novel compounds effective as leukotriene B_4 antagonists [I] having excellent pharmacological activities.

Another object of the present invention is to provide processes for producing those compounds [I]. A further object of the present invention is to provide a pharmaceutical composition containing a compound of the formula [I]. These and other objects will be apparent to those skilled in the art to which the present invention pertains from the foregoing and subsequent descriptions.

The novel leukotriene B_4 antagonists [I] of the invention can be prepared by the following methods:



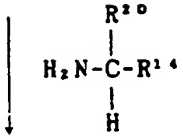




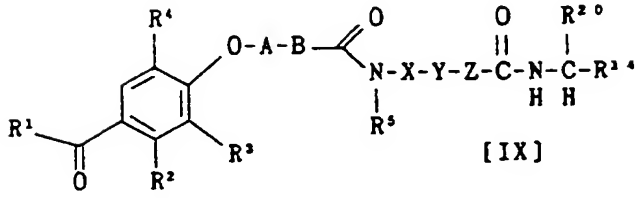
[VII]

Method A

Method B

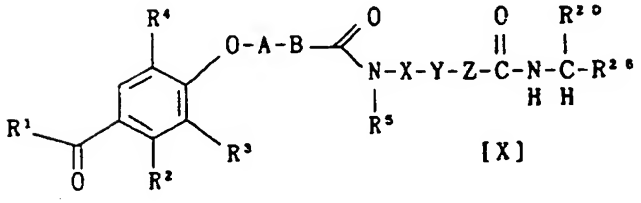


[VIII]

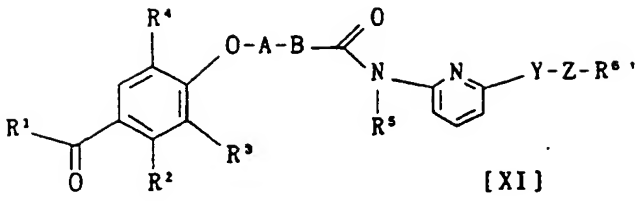


[IX]

Method C | NaOH

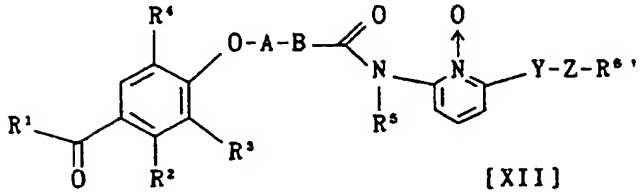


[X]

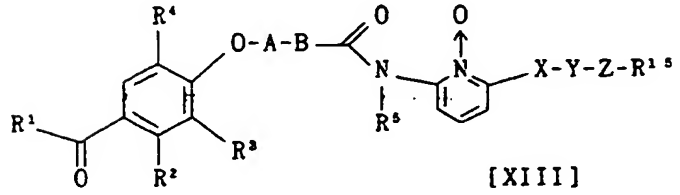


[XI]

Method D

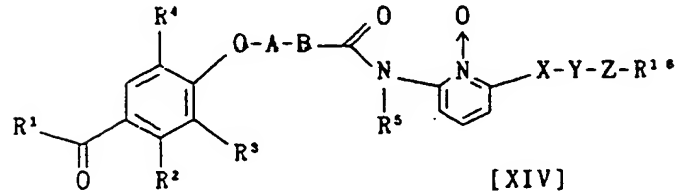


[XII]



[XIII]

Method C



[XIV]

(wherein A, B, R^1, R^2, R^3, R^4, R^5, $R^{6'}$, X, Y, Z and R^{20} are as defined above, and
R^{11} is the same as $R^{6'}$, but it does not mean free carboxylic group;
R^{12} is a group of the formula:

$X\text{-}Y\text{-}Z\text{-}COOR^{7'}$,
$X\text{-}Y\text{-}Z\text{-}CONHCHR^{20}(CH_2)_n\ COOR^{7'}$,
$X\text{-}Y\text{-}Z\text{-}CONHCHR^{20}CONHCHR^{22}CO_2R^{7'}$,
$CHR^{20}(CH_2)_nCOOR^{7'}$,
$CH_2CHR^{20}COOR^{7'}$, or
$CHR^{20}CONHCHR^{22}COOR^{7'}$,

wherein X, Y, Z, R^{20}, R^{22} and n are as defined above, and $R^{7'}$ is the same as R^7 but it does not mean a hydrogen atom,

R^{13} is a group of the formula:

X-Y-Z-COOH,
X-Y-Z-CONHCHR^{20}(CH$_2$)$_n$ COOH,
X-Y-Z-CONHCHR^{20}CONHCHR^{22}CO$_2$H,
CHR^{20}(CH$_2$)$_n$COOH,
CH$_2$CHR^{20}COOH, or
CHR^{20}CONHCHR^{22}COOH,

wherein X, Y, Z, R^{20}, R^{22} and n are as defined above.

R^{14} is a group of the formula:

(CH$_2$)$_n$COOR$^{7'}$, or
CONHCHR^{22}COOR$^{7'}$,

wherein $R^{7'}$, R^{22} and n are as defined above.

R^{15} is a group of the formula:

COOR$^{7'}$,
CONHCHR^{20}(CH$_2$)$_n$COOR$^{7'}$, or
CONHCHR^{20}CONHCHR^{22}CO$_2$R$^{7'}$,

wherein $R^{7'}$, R^{20}, R^{22} and n are as defined above.

R^{16} is a group of the formula:

COOH,
CONHCHR^{20}(CH$_2$)$_n$COOH, or
CONHCHR^{20}CONHCHR^{22}CO$_2$H,

wherein R^{20}, R^{22} and n are as defined above.

R^{26} is a group of the formula:

(CH$_2$)$_n$COOH, or
CONHCHR^{22}COOH,

wherein R^{22} and n are as defined above.

Method A

The amide compound [IV] or [IX] can be prepared from an acid compound [II] or [VII] by reacting an amine compound [III] or [VIII] in the presence of a condensing agent (e.g. dicyclohexylcarbodiimide, ethyldimethylaminopropylcarbodiimide hydrochloride, etc.), hydroxybenzotriazole and a tertiary amine (e.g. triethylamine, 4-dimethylaminopyridine, etc.) in an inert solvent (e.g. dichloromethane, mixed solvent of dichloromethane and N,N-dimethylformamide, etc.) at a temperature in the range from 0 °C to the boiling temperature of the solvent.

If a substituent of R^{20} of compound [VIII] is an impediment group (e.g. mercapto, carboxyl, amino group, etc.), the compound is previously protected by a protecting group (e.g. benzyl, benzyloxycarbonyl, t-butoxycarbonyl group, etc.), and after the reaction is carried out, the protecting group is eliminated. The protection and deprotection of R^{20} can be carried out by the conventional procedure. [Protective Group in Organic Chemistry, Edited by J. F. W. McOmic (1973) 95 - 143].

Method B

The amide compound [IV] or [IX] can be obtained from an acid chloride or an acid anhydride of an acid compound [II] or [VII] by reacting with an amine compound [III] or [VIII] in the presence of a tertiary amine (e.g. triethylamine, etc.), or by reacting with a salt of an amine compound [III] or [VIII] (e.g. sodium salt, potassium salt, etc.) in the absence of amine in an inert solvent (e.g. tetrahydrofuran, etc.) at a temperature in the range from 0 °C to a boiling temperature of the solvent.

The transformation of an acid group to an acid chloride group can be carried out by treating the acid compound with phosphorous oxychloride or thionyl chloride in an inert solvent (e.g. chloroform, etc.) or in the absence of solvent at a temperature in the range of from -40°C to the boiling temperature of the reaction mixture.

The transformation of an acid group to an acid anhydride group can be carried out by treating the acid compound with chloroformate ester (e.g. ethyl chloroformate, etc.) in the presence of a tertiary amine (e.g. triethylamine, etc.) in an inert solvent (e.g. chloroform, etc.) at a temperature in the range of from -40 °C to the boiling temperature of the solvent.

If a substituent of R^{20} of compound [VIII] is a impediment group (e.g. mercapto, carboxyl, amino group, etc.), the compound is previously protected by a protecting group (e.g. benzyl group, benzyloxycarbonyl group, t-butoxycarbonyl group, etc.), and after the reaction is carried out, the protecting group is eliminated.

The protection and deprotection of R^{20} can be carried out by the conventional procedure [Protective Group in Organic Chemistry, Edited by J. F. W. McOmic (1973) 95 - 143].

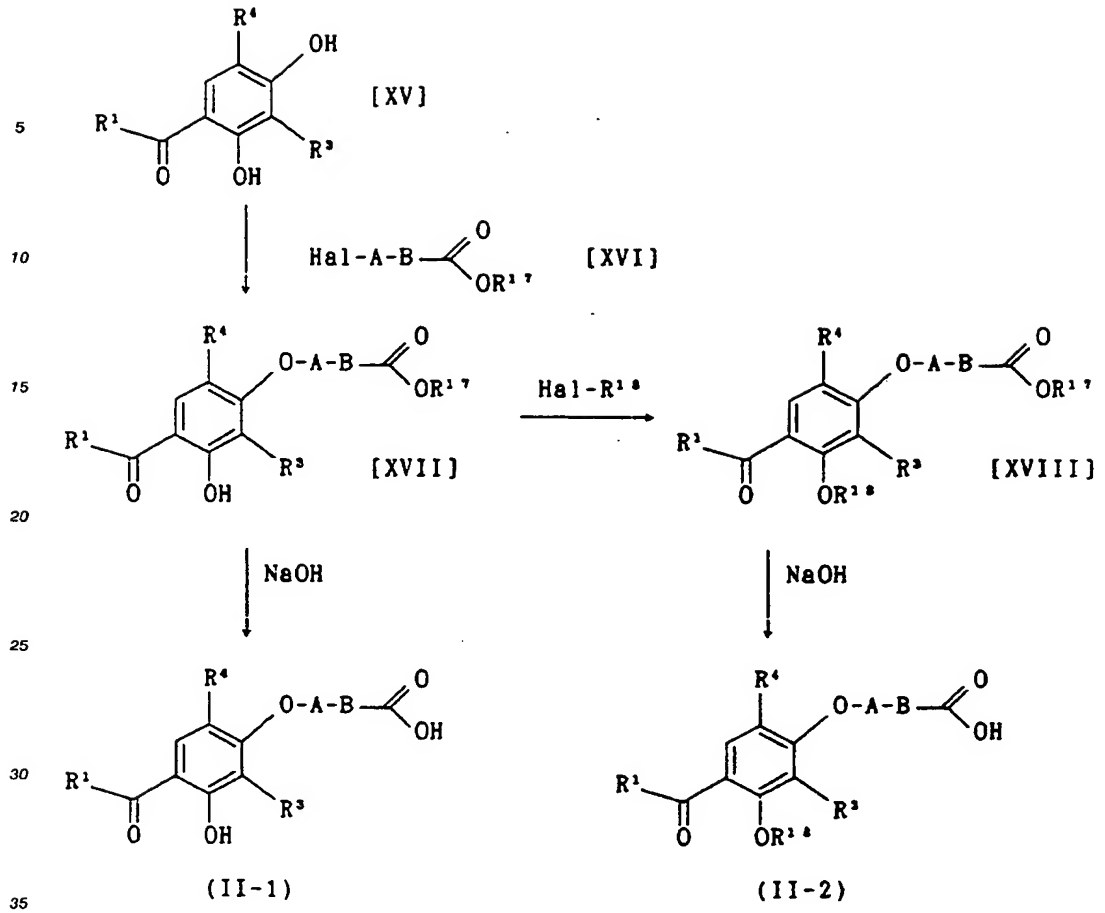
Method C

The acid compound [VI], [X] or [XIV] can be prepared by hydrolysis of the ester compound [V], [IX) or [XIII] by treating with an aqueous alkali (e.g. sodium hydroxide, lithium hydroxide) in an inert solvent (e.g. tetrahydrofuran, methanol, ethanol, etc.).

Method D

The N-oxide compound [XII] can be prepared from pyridine compound [XI] by treating with an oxidizing agent (e.g. m-chloroperbenzoic acid, etc.) in an inert solvent (e.g. methylene chloride, etc.).

The amine compounds [III] and [VIII] are known compounds or easily obtained as described in e.g. J. Goto, K. Sakane, Y. Nakai, T. Teraji, The journal of antibiotics, 37, 532 (1984), I. Csendes, B. W. Müller, W. Tosch, The journal of antibiotics, 36, 1020 (1983), M. Ohta, Yakugaku zassi, 72, 1536 (1983), JP-A-58-23697. And, the starting compounds [II], [II-1] and [II-2] can be obtained by the following method.



(wherein A, B, R^1 , R^2 , R^3 and R^4 are as defined above, R^{17} is a C_1-C_5 alkyl group, R^{18} is a C_1-C_5 alkyl group, Hal is a chlorine or bromine atom)

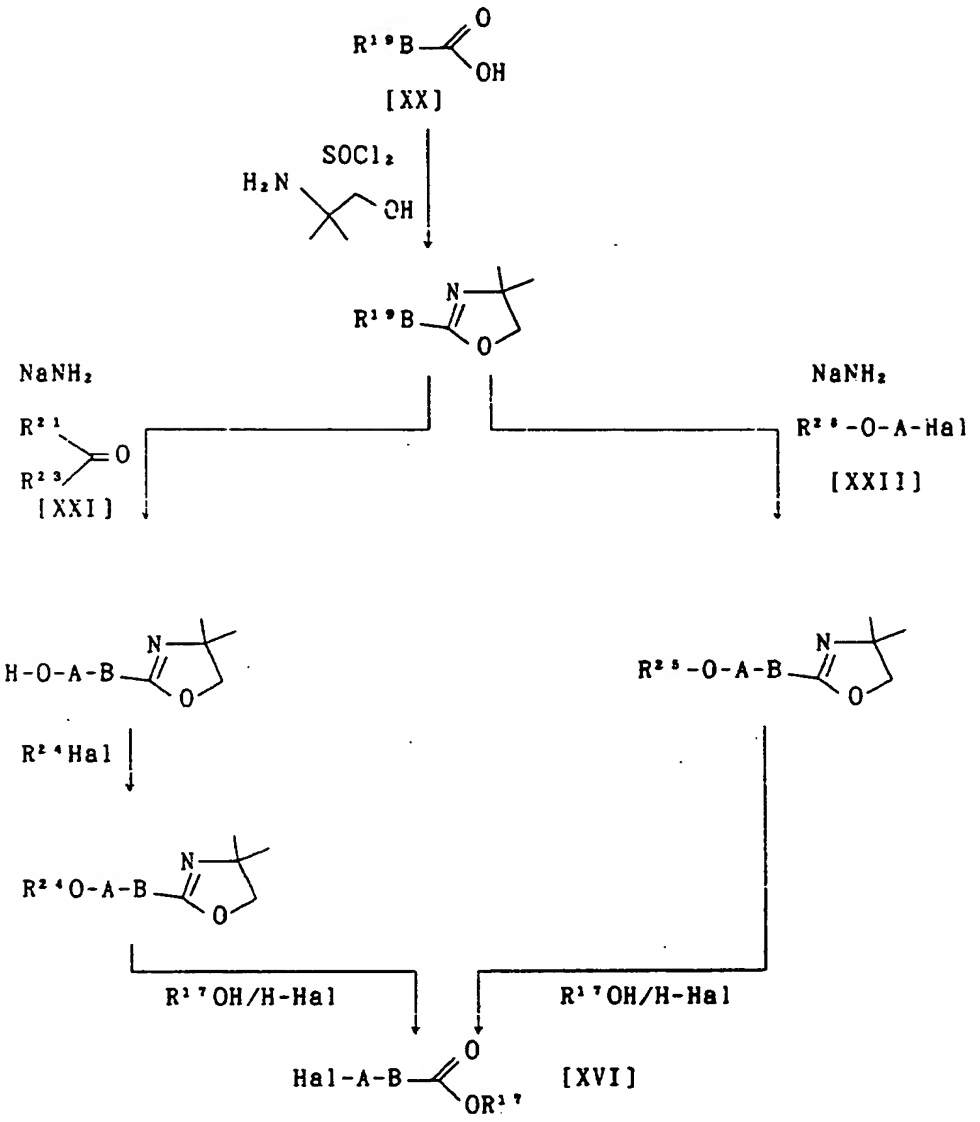
Alkylation of the compound [XV] into the compound [XVII] can be accomplished by treating the former with the compound [XVI] in an inert solvent (e.g. N,N-dimethylformamide, etc.) in the presence of a base (e.g. anhydrous potassium carbonate, etc.). Optionally, the compound [XVII] can be alkylated to produce the compound [XVIII] by the same procedure as used in the synthesis of the compound [XVII] from the compound [XV]. And, the compound (II-1) and (II-2), respectively, can be prepared from the compound [XVII] and [XVIII] by hydrolysis (Method C).

The compound [XV] is a known compound or easily obtained as described in e.g. J. Hurst, J. Wibberley, Journal of Chemical Society, 1962, 119.

The compound [XVI] is obtained by;

(1) In the case where both Hal and B of compound [XVI] are jointed to the same carbon atom:
the compound [XVI] is a known compound or easily obtained as described in e.g. J. Hurst, J. Wibberley, Journal of Chemical Society, 1962, 119, etc,

(2) In the case that there are two carbon atoms between Hal and B in compound [XVI]:

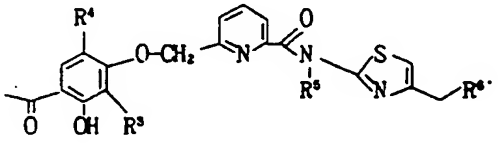


(wherein A, B and Hal are as defined above, R^{19} is a C_1-C_5 alkyl group (but, there is at least one hydrogen atom at the α carbon bonded to B), R^{21}, R^{23} are each independently a hydrogen atom or a C_1-C_5 alkyl group, R^{24} is a C_1-C_5 alkyl group, and R^{25} is a C_1-C_5 alkyl group or phenyl group)
the compound [XVI] is prepared in the following way:
first step: the carboxylic acid group of a compound [XX] is protected to yield a 4,4-dimethyl-2-oxazoline compound,
second step: the 4,4-dimethyl-2-oxazoline compound is treated with a base to deprotonate a hydrogen atom attached to a carbon atom adjacent to B group (e.g. sodium amide, n-butyl lithium, etc.),
third step: the deprotected compound is reacted with the compound of the formula [XXI] (aldehyde or ketone) to yield a hydroxy compound,
fourth step: the hydroxyl compound is alkylated by reacting with a compound of the formula R^{24}-Hal,
fifth step: the alkylated compound is treated with halogenated hydrogen (e.g. hydrogen chloride, hydrogen bromide, etc.) in the alcohol represented by $R^{17}OH$.

(3) In the case that there are 3 or more carbon atoms between Hal and B in the compound [XVI]: the compound [XVI] is prepared in the same way, except modifying the alkylation reaction, as described in above (2), i.e., the compound [XX] is protected and deprotonated, and then alkylated by alkylhalide [XXII]. The alkylated product is treated with halogenated hydrogen (e.g. hydrogen chloride, hydrogen bromide, etc.) in the alcohol represented by $R^{17}OH$.

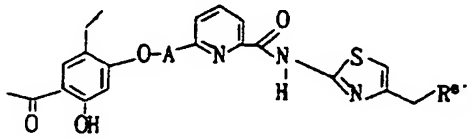
Specific examples of the leukotriene B_4 antagonists are as follows:

Table 1



R^3	H	H	H	n-Pr	H	H	H	H	H
R^4	Me	n-Pr	n-Pr	H	Et	Et	Et	Et	Et
R^5	H	H	H	H	CH_3	Et	n-Pr	I-Pr	H
$R^{6'}$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	CONHMe

Table 2



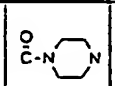
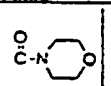
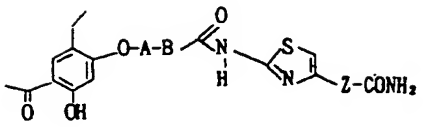
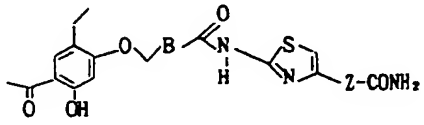
A	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-(CH_2)_5-$
$R^{6'}$	$CONMe_2$	CONHiPr				$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$

Table 3



A	-CHMe-	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$
B									
Z	$-CH_2-$	single bond	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-(CH_2)_5-$	$-CH_2-$	single bond

Table 4



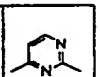
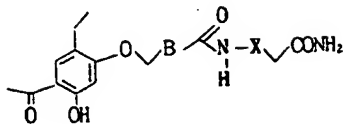
B									
Z	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	single bond	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$

Table 5



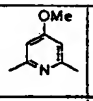
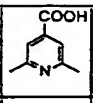
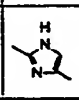
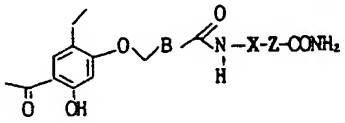
B									
X									

Table 6



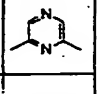
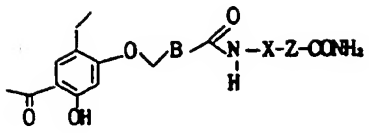
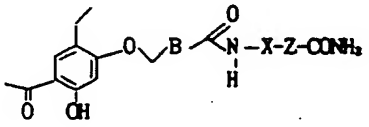
B									
X									
Z	single bond	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	single bond	$-CH_2-$	$-(CH_2)_2-$	single bond

Table 7



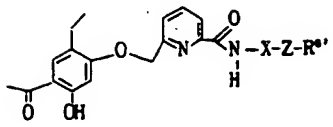
B									
X									
Z	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	single bond	$-CH_2-$	$-(CH_2)_2-$	single bond	$-CH_2-$

Table 8



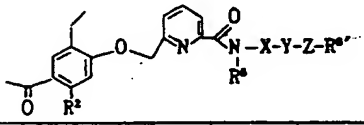
B									
X									
Z	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-CH_2-$	single bond	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-CMe_2-$

Table 9



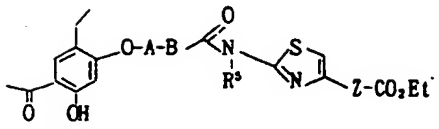
X									
Z	single bond	single bond	single bond	single bond	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$
$R^{6'}$	$CONH_2$	$CONH_2$	SO_2NH_2	SO_2NH_2	$CONH_2$	$CONH_2$	SO_2NH_2	SO_2NH_2	SO_2NH_2

Table 10



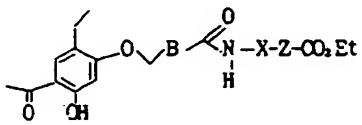
R^2	OH	OH	OH	OH	OMe	OH	OH	OH	OH
R^5	H	H	H	H	H	H	Me	Et	n-Pr
X									
Y	-O-	-O-	-O-	-O-	single bond	single bond	single bond	single bond	single bond
Z	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$
$R^{5'}$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	$CONH_2$	CO_2Et	CO_2Et	CO_2Et	CO_2Et

Table 11



A	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-(CH_2)_5-$	-CHMe-	$-CH_2-$	$-CH_2-$	$-CH_2-$
B									
R^5	i-Pr	H	H	H	H	H	H	H	H
Z	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$

Table 12



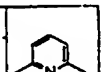
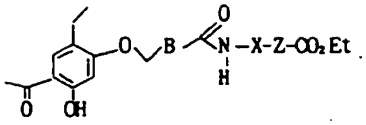
B									
X									
Z	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-CH_2-$	$-CH_2-$

Table 13



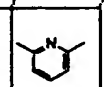
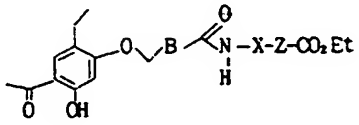
B									
X									
Z	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$

Table 14



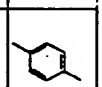
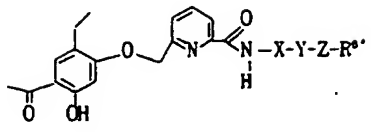
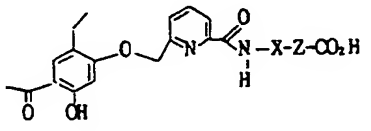
B									
X									
Z	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_2-$

Table 15



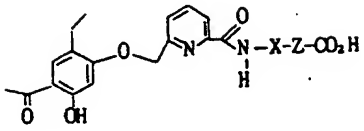
X									
Y	-O-	-O-	-O-	-O-	single bond	single bond	single bond	single bond	single bond
Z	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_2-$	single bond	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$
$R^{6'}$	CO_2Et	CO_2Et	CO_2Et	CO_2Et	CO_2H	CO_2H	CO_2H	CO_2H	CO_2H

Table 16



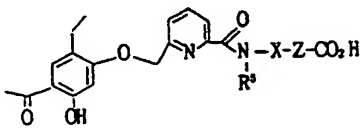
X									
Z	$-(CH_2)_5-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$	$-(CH_2)_2-$

Table 17



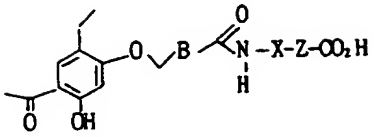
X									
Z	$-CH_2-$	$-(CH_2)_2-$	single bond	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-(CH_2)_4-$	$-(CH_2)_5-$	single bond

Table 18



R^5	H	H	H	Me	Et	n-Pr	i-Pr	n-Bu	i-Bu
X									
Z	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$

Table 19



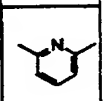
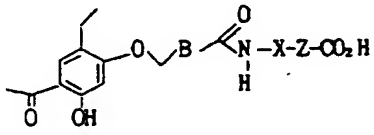
B									
X									
Z	-CH_2-	-$(CH_2)_2$-	-CH_2-	-$(CH_2)_2$-	-CH_2-	-$(CH_2)_2$-	-$(CH_2)_3$-	-CH_2-	-$(CH_2)_2$-

Table 20



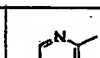
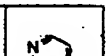
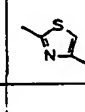
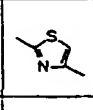
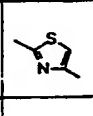
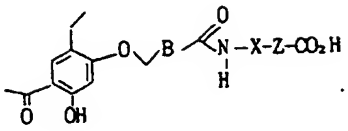
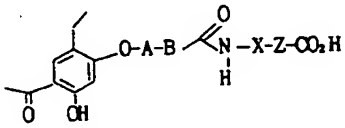
B									
X									
Z	-$(CH_2)_3$-	-CH_2-	-$(CH_2)_2$-	-$(CH_2)_3$-	-CH_2-	-$(CH_2)_2$-	-$(CH_2)_3$-	-CH_2-	-$(CH_2)_2$-

Table 21



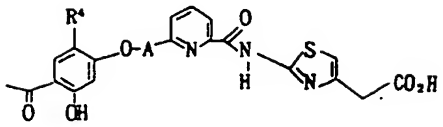
B									
X									
Z	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$

Table 22



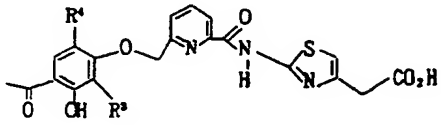
A	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$
B									
X									
Z	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-(CH_2)_2-$	$-(CH_2)_3-$	$-CH_2-$	$-CH_2-$

Table 23



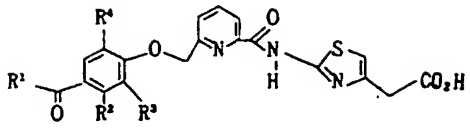
R^4	Et	Et	Et	Me	Et	n-Pr	n-Bu	$-CH_2-CH=CH_2$	$CH_2C\equiv CH$
A	$-(CH_2)_4-$	$-(CH_2)_5-$	-CHMe-	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-CH_2-$

Table 24



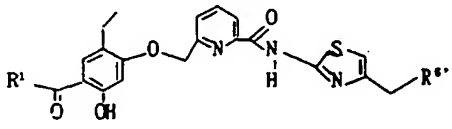
R^3	Me	Et	n-Pr	n-Bu	n-Pentyl	$-CH_2-CH=CH_2$	$CH_2C\equiv CH$	Me	Et
R^4	Et	Et	Et	Et	Et	Et	Et	H	H

Table 25



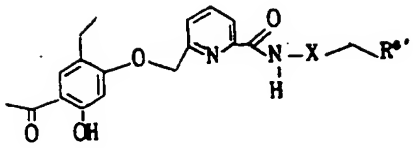
R^1	Me	Me	Me	Me	Me	Me	Me	Et	n-Pr
R^2	OH	OH	OH	OH	OMe	OEt	O-n-Pr	OH	OH
R^3	i-Pr	i-Bu	n-Bu	n-Pentyl	H	H	H	H	H
R^4	H	H	H	H	Et	Et	Et	Et	Et

Table 26



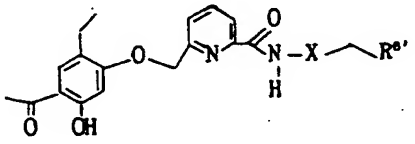
R^1	n-Bu	n-Pentyl	Me	Me	Me
$R^{6'}$	CO_2H	CO_2H	$\overset{O}{\overset{\|}{C}}N\text{-}CH_2CO_2Me$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}(CH_2)_3CO_2Me$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}CH_2CO_2H$ (H)

Table 27



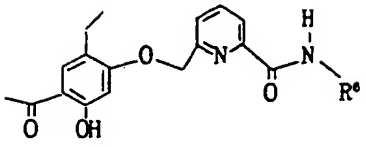
X					
$R^{6'}$	$\overset{O}{\overset{\|}{C}}N\text{-}(CH_2)_2CO_2H$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}CH_2CO_2Me$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}(CH_2)_2CO_2Me$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}CH_2CO_2H$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}(CH_2)_2CO_2H$ (H)

Table 28



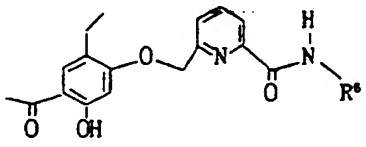
X					
$R^{6'}$	$\overset{O}{\overset{\|}{C}}N\text{-}(CH_2)_3CO_2H$ (H)	$\overset{O}{\overset{\|}{C}}N\text{-}\underset{H}{C}HCO_2Me$ (^{i}Pr)	$\overset{O}{\overset{\|}{C}}N\text{-}\underset{H}{C}HCH_2CO_2H$	$\overset{O}{\overset{\|}{C}}N\text{-}\underset{H}{C}HCO_2H$ ($(CH_2)_4NH_2$)	$\overset{O}{\overset{\|}{C}}N\text{-}\underset{H}{C}HCO_2H$ (CH_2OH)

Table 29



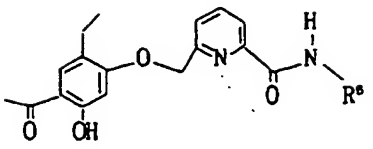
R^6	CH_2CO_2H	$(CH_2)_2CO_2H$	$(CH_2)_3CO_2H$	$(CH_2)_4CO_2H$	CH_2CO_2Me

Table 30



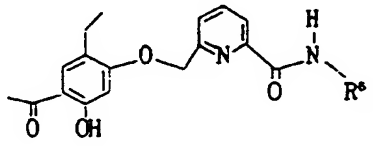
R^6	CH_2CO_2Et	$CH_2CO_2CH_2$- 	$CHCO_2H$ CH_3	$CHCO_2H$	$CHCO_2H$ 

Table 31



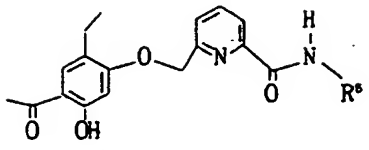
R^6	$CHCO_2H$	$CHCO_2H$	$CHCO_2H$	$CHCO_2H$	$CHCO_2H$
	$CH(CH_3)_2$	Ph	CH_2Ph	CH_2-(4-OH-Ph)	CH_2OH

Table 32



R^6	CH_2CO_2H	CH_2CO_2H	CH_2CO_2H	CH_2CO_2H	$CHCO_2H$
	$CH(OH)CH_3$	CH_2CH_2OH	CH_2CH_2SMe	CH_2SH	$(CH_2)_4NH_2$

Table 33



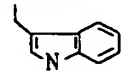
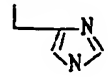
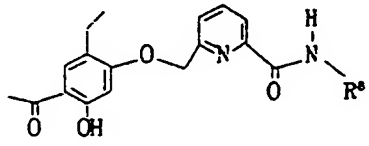
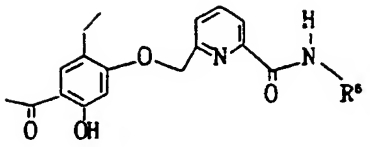
R^6	$CHCO_2H$  H	$CHCO_2H$  H	$CHCO_2H$ CH_2CO_2H	$CHCO_2H$ $CH_2CH_2CO_2H$	$CHCO_2H$ $CH_2CH_2CONH_2$

Table 34



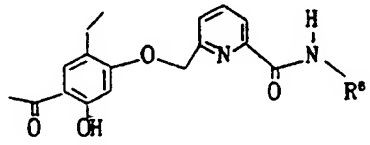
R^6	$CHCO_2H$ CH_2CONH_2	$CHCO_2H$ $(CH_2)_4NHCNH_2$ NH	CH_2CONH_2	$CH_2CONHCH_3$	CH_2CONMe_2

Table 35



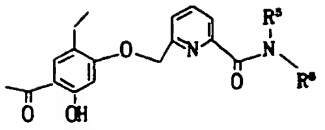
R^6	$(CH_2)_2CONH_2$	$(CH_2)_3CONMe_2$	CH_2CON ⬡	CH_2CON ⬡O	CH_2CON ⬠

Table 36



R^6	$CHCONH_2$ | CH_3	$CHCONH_2$ ⟙	$CHCONMe_2$ ⬡	$CHCONMe_2$ | OH	$CHCONHMe$ | OH

Table 37



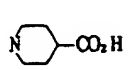
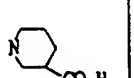
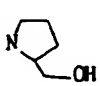
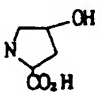
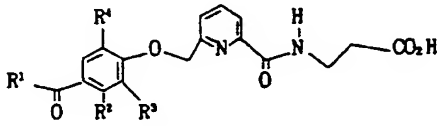
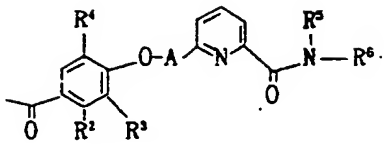
R^5, R^6					
					

Table 38



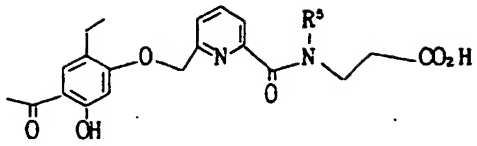
R^1	Et	n-Pr	Me	Me	Me
R^2	OH	OH	OMe	OEt	OH
R^3	H	H	H	H	n-Pr
R^4	Et	Et	Et	Et	H

Table 39



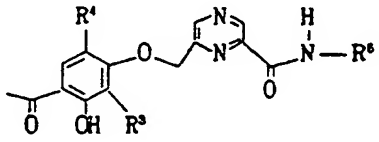
R^2	OH	OMe	OMe	OH	OH
R^3	n-Pr	n-Pr	n-Pr	H	H
R^4	H	H	H	Et	Et
A	$-CH_2-$	$-CH_2-$	$-CH_2-$	$-(CH_2)_2-$	$-CH_2-$
R^5	H	H	H	H	Me
R^6	$CHCO_2H$ CH_3	$CHCO_2H$ CH_3	$(CH_2)_2CO_2H$	$(CH_2)_2CO_2H$	$(CH_2)_2CO_2H$

Table 40



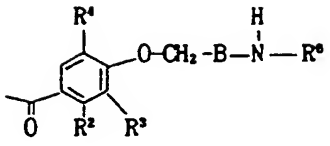
R^5	Et	n-Pr	isoBu	sec-Bu	$(CH_2)_2OH$

Table 41



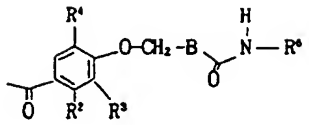
R^3	H	H	H	H	n-Pr
R^4	Et	Et	Et	Et	H
R^6	$(CH_2)_2CO_2H$	$CHCO_2H$ CH_3	$CHCO_2H$ CH_2OH	$CHCO_2H$ CH_2CO_2H	$CHCO_2H$ CH_2CO_2H

Table 42



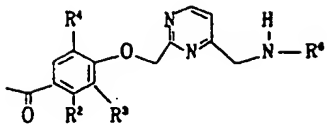
R^2	OMe	OH	OH	OH	OH
R^3	n-Pr	H	H	H	H
R^4	H	Et	Et	Et	Et
B					
R^6	$CH(CO_2H)CH_2CO_2H$	$(CH_2)_2CO_2H$	$CH(CO_2H)CH_3$	$CH(CO_2H)CH_2OH$	$CH(CO_2H)CH_2CO_2H$

Table 43



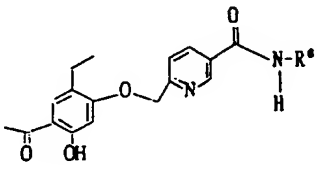
R^2	OH	OMe	OH	OH	OH
R^3	n-Pr	n-Pr	H	H	H
R^4	H	H	Et	Et	Et
B					
R^5	$CHCO_2H$ CH_2CO_2H	$CHCO_2H$ CH_2CO_2H	$(CH_2)_2CO_2H$	$CHCO_2H$ CH_3	$CHCO_2H$ CH_2OH

Table 44



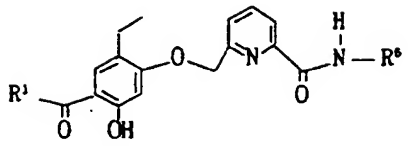
R^2	OH	OH	OMe	OH	OH
R^3	H	n-Pr	n-Pr	H	H
R^4	Et	H	H	Et	Et
R^6					

Table 45



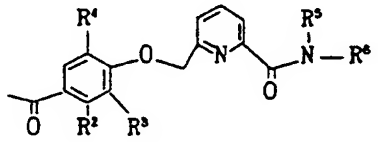
R^6					

Table 46



R^1	Me	Et	Me	Me	Me
R^6	$(CH_2)_2OH$	$(CH_2)_3OH$	$(CH_2)_4OH$	$CHCH_2OH$ | CH_3	$CHCH_2OH$ | CH_2CH_3

Table 47



R^2	OH	O-n-Pr	OH	OH	OH
R^3	Me	H	H	H	H
R^4	Me	H	Et	Et	Et
R^5	H	H	H	Me	H
R^6	$(CH_2)_2CO_2H$	$(CH_2)_2CO_2H$	$CH(CH_2OH)_2$	$CH(CH_2OH)_2$	$CH_2CONHCH_2CO_2H$

Among the leukotriene B_4 antagonists thus obtained, the compound [I] can be converted to a pharmaceutically acceptable salt form. The pharmaceutically acceptable salts of these leukotriene B_4 antagonists can be formed with pharmaceutically acceptable metal cation such as sodium, potassium, magnesium and calcium, ammonium or amine cations.

The preparations of pharmaceutical compositions can be carried out by conventional methods. For

example, leukotriene B_4 antagonists [I] may be mixed with carriers, diluents, lubricants, fillers and/or binders such as lactose, sucrose, calcium phosphate, starch, talcum, casein, magnesium stearate, methyl cellulose, polyglycols, tragacanth and the like, sometimes together with stabilizers and emulsifying agents. The resulting mixture may be processed in a usual manner to tablets, capsules, pills, injections, ointment, suppositories and the like. In a clinical practice, the leukotriene B_4 antagonists [I] can be administered orally, intranasally, intradermally or the like.

The daily dosage may vary depending upon the administration route, symptom, age or weight of the patient, and the usual oral dosage of the active ingredient is between about 1 mg and about 1000 mg daily for human beings.

DESCRIPTION OF THE PREFERED EMBODIMENTS

Practical and prefered embodiments of the present invention are illusturated in the following examples, which are not intended to limit the scope of the invention.

Reference Example 1

5-Ethyl-2,4-dihydroxyacetophenone (0.97 g, 5.0 mmol) and methyl 6-bromomethylpyridine-2-carboxylate (1.38 g, 5.8 mmol) were dissolved in an N,N-dimethylformamide solution (50 ml), and anhydrous potassium carbonate (480 mg) was added to the above solution, and the mixture was stirred at room temperature for 16 hours. The reaction mixture was poured into water and extracted with ethyl acetate (100 ml × 3).

The extract was dried, concentrated and chromatographed on silica gel to give methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylate.

Reference Example 2

Methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy) methyl]pyridine-2-carboxylate (38 mg, 12 mmol) was dissolved in a methanol solution (2 ml), and one normal sodium hydroxide (1 ml) was added to the above solution at 0 °C, and the mixture was stirred at room temperature for 1 hour. One-tenth normal potassium bisulfate was titrated to the above solution until it became pH2. Then, precipitated white crystals were filtered off, and washed with water, and dried to give 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylic acid.

Reference Example 3

3-n-Propyl-2,4-dihydroxyacetophenone (816 mg, 4.2 mmol) was added to a methanol solution (10 ml), sodium metal was added to the solution at 0 °C, and the mixture was stirred for 30 min, and evaporated under reduced pressure, and dried to give a sodium salt of 3-n-propyl-2.4-dihydroxyacetophenone. The salt was dissolved in N,N-dimethylformamide (10 ml), and it was added to a N,N-dimenthylformamide solution (10 ml) of methyl-6-bromo-methylpyridine-2-carboxylate (920 mg, 4.0 mmol) at room temperature, and the mixture was stirred for 1 hour.

The reaction mixture was poured into water, and normal potassium bisulfate was titrated until it became pH3, and extracted with ethyl acetate (100 ml × 3). The extract was dried, concentrated and chromatographed on silica gel to give methyl 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)methyl]pyridine-2-carboxylate.

Reference Example 4

According to the procedure of Reference Example 2, 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)methyl]-pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-3-hydroxy-2-n-propylphenoxy)-methyl]pyridine-2-carboxylate.

Reference Example 5

Anhydrous potassium carbonate (1.0 g) was added to a N,N-dimethylformamide solution (10 ml) of methyl 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylate (500 mg, 1.4 mmol) and methyliodide (5 ml),and the mixture was stirrered at 70 °C for 2 hours.

The reaction mixture was poured into water and extracted with ethylacetate and washed with saturated aqueous sodium chloride. Then, the extract was dried, concentrated and chromatographed on silica gel to

give methyl 6-[(4-acetyl-2-ethyl-5-methoxyphenoxy)methyl]pyridine-2-carboxylate.

Reference Example 6

According to the procedure of Reference Example 2, 6-[(4-acetyl-2-ethyl-5-methoxyphenoxy)methyl]-pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-2-ethyl-5-methoxy-phenoxy)-methyl]pyridine-2-carboxylate.

Reference Example 7

According to the procedure of Reference Example 5, methyl 6-[(4-acetyl-2-n-propyl-3-methoxy-phenoxy)methyl]pyridine-2-carboxylate was obtained from methyl 6-[(4-acetyl-3-hydroxy-2-n-propyl-phenoxy)methyl]pyridine-2-carboxylate.

Reference Example 8

According to the procedure of Reference Example 2, 6-[(4-acetyl-2-n-propyl-3-methoxyphenoxy)-methyl]pyridine-2-carboxylic acid was obtained by hydrolysis of methyl 6-[(4-acetyl-2-n-propyl-3-metho-xyphenoxy)methyl]pyridine-2-carboxylate.

Reference Example 9 (a compound included in formula [XVI])

A mixture of 6-methylpyridine-2-carboxylic acid (13.7 g, 100 mmol) and thionyl chloride (40 ml) was stirred at 70 °C for 1 hour. The mixture was dried, and dichloromethane (40 ml) was added to the residue. The solution was added to a dichloromethane solution of 2-amino-2-methyl-propanol (36.0 g, 400 mmol), and stirred. The mixture was washed with water, and dried over anhydrous magnesium sulfate. The extract was concentrated and chromatographed on silica gel to give an amide compound. 4,4-Dimethyl-2-oxazoline compound was obtained by reacting the amide compound and thionyl chloride in dichloromethane. 4,4-Dimethyl-2-oxazoline compound was reacted with n-butyl lithium at 78 °C in anhydrous tetrahydrofuran, and chlorophenyl ether (782 mg, 5 mmol) was added. Purified alkylated compound was treated with ethanol saturated with HCl to give ethyl 6-(3-chloropropyl)-pyridine-2-carboxylate.

Reference Example 10 (a compound included in formula [II])

According to the procedure of Reference Examples 1,2, 6-[3-(4-acetyl-2-ethyl-5-hydroxyphenoxy)-propyl]pyridine-2-carboxylic acid was obtained from ethyl 6-(3-chloropropyl)pyridine-2-carboxylate and 5-ethyl-2,4-dihydroxyacetophenone.

Table 48

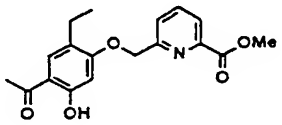
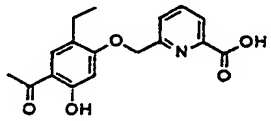
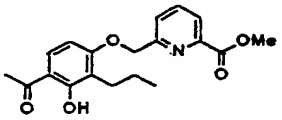
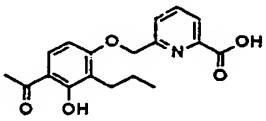
1	
2	
3	
4	

Table 49

	^{1}H-NMR	δppm
1	(solvent:$CDCL_3$) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 4.04(3H,s), 5.39(2H,s), 6.46(1H,d,J = 8.9Hz), 7.59(1H,d,J = 8.9Hz), 7.79(1H,d,J = 6.6Hz), 7.92(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.10(1H,d,J = 7.9Hz)	
2	(solvent:$CDCL_3$) 1.26(3H,t,J = 7.6Hz), 2.59(3H,S), 2.68(2H,q,J = 7.6Hz), 5.30(2H,s), 6.43(1H,s), 7.51(1H,s), 7.78(1H,d,J = 6.9Hz), 8.04(1H,dd,J = 6.9Hz,J = 7.9Hz), 8.22(1H,d,J = 7.9Hz)	
3	(solvent:$CDCL_3$) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 4.04(3H,s), 5.39(2H,s), 6.46(1H,d,J = 8.9Hz), 7.59(1H,d,J = 8.9Hz), 7.79(1H,d,J = 6.6Hz), 7.92(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.10(1H,d,J = 7.9Hz)	
4	(solvent:$CDCL_3$) 0.99(3H,t,J = 7.4Hz), 1.62(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.57(3H,s), 2.76(2H,t,J = 7.4Hz), 5.34(2H,s), 6.45(1H,d,J = 8.9 Hz), 7.60(1H,d,J = 8.9Hz), 7.79(1H,dd,J = 1.0Hz,J = 6.9Hz), 8.04(1H, dd,J = 6.9Hz,J = 7.4Hz), 8.21(1H,dd J = 1.0Hz, J = 7.4Hz)	

Table 50

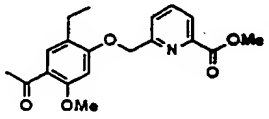
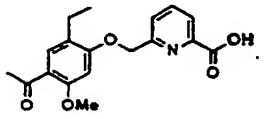
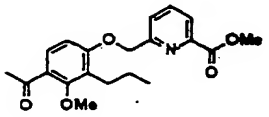
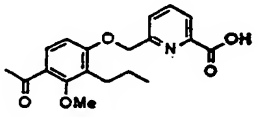
5	
6	
7	
8	

Table 51

	^{1}H-NMR	δppm
5	(solvent:$CDCl_3$) 1.24(3H,t,J = 7.6Hz), 2.58(3H,s), 2.70(2H,q,J = 7.6Hz), 3.86(3H,s), 4.04(3H,s), 5.40(2H,s), 7.72(1H,s), 7.79(1H,d,J = 7.9Hz), 7.94(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.11(1H,d,J = 7.6Hz)	
6	(solvent:$CDCl_3$) 1.24(3H,t,J = 7.4Hz),2.57(3H,s), 2.69(2H,q,J = 7.4Hz), 3.90(3H,s), 5.40(2H,s), 6.64(1H,s), 7.65(1H,s), 7.80(1H,d,J = 7.3Hz), 8.01(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.13(1H,d,J = 7.9Hz)	
7	(solvent:$CDCl_3$) 1.02(3H,t,J = 7.5Hz), 1.66(2H,q,J = 7.6Hz), 2.61(3H,s), 2.75(2H,t,J = 7.8Hz), 3.78(3H,s), 5.31(2H,s), 6.70(1H,d,J = 8.6Hz), 7.56(1H,d,J = 8.9Hz), 7.90(1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.21(1H,d,J = 7.6Hz)	
8	(solvent:$CDCl_3$) 1.02(3H,t,J = 7.6Hz), 1.65(2H,q,J = 7.7Hz), 2.62(3H,s), 2.75(2H,t,J = 7.8Hz), 3.78(3H,s), 5.31(2H,s), 6.70(1H,d,J = 8.6Hz), 7.56(1H,d,J = 8.9Hz), 7.90(1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.21(1H,d,J = 7.6Hz)	

Example 1

A mixture of 6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxylic acid (63 mg, 0.20 mmol), 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (40 mg, 0.20 mmol), 1-hydroxybenzotriazole (30 ml, 0.22 mmol), 2-aminothiazole-4-carboxamide (35 mg, 0.24 mg) and triethylamine (20 mg), 0.20 mmol) in a mixed solution of dichloromethane (2 ml) and N,N-dimethylformamide (2 ml) was stirred at room temperature for 44 hours. The reaction mixture was poured into water and extracted with ethyl acetate (80 ml×3). The extract was dried over anhydrous magnesium sulfate, concentrated under reduced pressure and chromatographed on silica gel to give 2[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)-methyl]pyridine-2-carboxamide]thiazol-4-ylcarboxamide.

Example 2~35,62,88,90,92

According to the procedure of Example 1, the compounds (Example 2~ 35,62,88,90,92) were obtained.

Example 36

Ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyride-2-carboxamide]thiazole-4-ylcarboxylate (24 mg, 0.05 mmol) was suspended in methanol (1.5 ml), followed by addition of one-second normal sodium hydroxide (1.0 ml).

After the solution was stirred for 2 hr, it was made acidic with one-second normal potassium bisulfate. Precipitated crystals were separated by filtration, and washed with water, and dried to give 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]thizaol-4-ylcarboxylic acid.

Example 37~52,61,87,89,91

According to the procedure of Example 36, the compounds (Example 37 ~52, 61, 87, 89, 91) were obtained.

Example 54~56,64,67,68,70,72,74,76,78,80,82,84,86,94,96,100, 102,104,106,108,112,114,115,116-121,123,126,127,138,141

According to the procedure of Example 1, the title compounds were obtained.

Example 53,57~60,63,65,69,71,73,75,77,79,81,83,85,93,95,99, 101,105,107,111,113,122,130

According to the procedure of Example 36, the title compounds were obtained.

Example 98

Ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]pyridine-2-carboxamide]pyridine-6-ylcarboxylate (280 mg, 0.60 mM) was dissolved in dichloromethane (5 ml), followed by addition of m-chloroperbenzoic acid (124 mg, 0.72 mM). After being stirred at room temperature for 16 hours, the reaction mixture was washed with aqueous sodium sulfite-sodium bicarbonate, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give ethyl 2-[6-[(4-acetyl-2-ethyl-5-hydroxyphenoxy)methyl]-pyridine-2-carboxamide]pyridine-N-oxide-6-ylcarboxylate.

Example 110,125,129,131,134,136,139,142

According to the procedure of Example 98, the title compounds were obtained.

Example 97,109,124,128,132,133,135,137,140

According to the procedure of Example 36, the title compounds were obtained.

Example 143–178, 212,214,216,218,222,225,226

According to the procedure of Example 1, the title compounds were obtained.

Example 179–211,213,215,223,224

According to the procedure of Example 36, the title compounds were obtained.

Table 52

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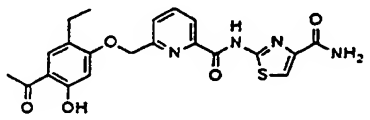
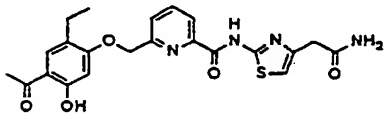
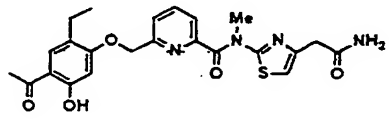
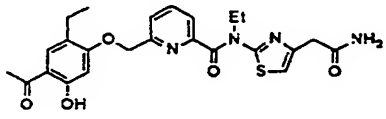
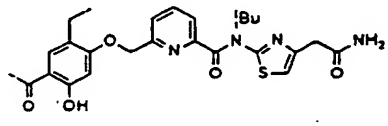
1	
2	
3	
4	
5	

Table 53

	^{1}H-NMR	δppm
1	(solvent:$CDCL_3$) 1.28(3H,t,J = 7.6Hz, 2.60(3H,s), 2.71(2H,q,J = 7.6Hz), 5.34(1H,s), 5.55(1H,bs), 6.48(1H,s), 7.05(1H,bs), 7.52(1H,s), 7.77(1H,d,J = 7.3Hz, 9.90(1H,s), 8.04 (1H,dd,J = 6.6Hz, J = 7.3Hz), 8.28(1H,d,J = 7.3Hz), 10.98(1H,bs), 12.70(1H,s)	
2	(solvent:$CDCL_3$) 1.27(3H,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.69(2H,s), 5.32(2H,s), 5.43(1H,bs), 6.45(1H,s), 6.60(1H,bs), 6.86(1H,s), 7.51(1H,s), 7.74(1H,d,J = 6.9Hz), 8.02(1H,t,J = 6.9Hz), 8.27(1H,d,J = 6.9Hz), 12.68(1H,s)	
3	(solvent:$CDCL_3$) 1.26(3H,t,J = 7.6Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.70(2H,s), 3.81(3H,s), 5.39(1H,s), 5.43(1H,bs), 6.46(1H,s), 6.70(1H,bs), 6.88(1H,s), 7.49(1H,s), 7.64(1H,dd,J = 1.0Hz,J = 7.9Hz), 7.79(1H,dd,J = 7.6Hz,J = 7.9Hz), 7.95(1H,dd,J = 1.0Hz,J = 7.6Hz), 12.65(1H,s)	
4	(solvent:$CDCL_3$) 1.26(3H,t,J = 7.6Hz, 1.44(3H,t,J = 6.9Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.69(2H,S), 4.36(2H,q,J = 6.9Hz) 5.25(1H,s), 5.44(1H,bs), 6.43(1H,s), 6.67(1H,bs), 6.89(1H,s), 7.49(1H,s), 7.64(1H,d,J = 7.9Hz), 7.74(1H,d,J = 6.9Hz), 7.94(1H,dd,J = 6.9Hz),J = 7.9Hz), 12.66(1H,s)	
5	(solvent:$CDCL_3$) 0.78(6H,d,J = 6.6Hz), 1.26(3H,t,J = 7.6Hz), 2.0-2.2(1H,m), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.66(2H,s), 4.33(2H,d,J = 7.3Hz), 5.21(2H,s), 5.84(1H,bs), 6.42(1H,s), 6.60(1H,bs), 6.88(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.74(1H,d,J = 7.9Hz), 7.93(1H,dd,J = 6Hz,J = 7.9Hz), 12.66(1H,s)	

Table 54

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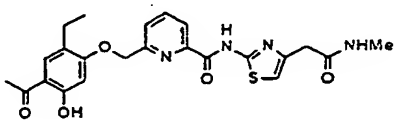
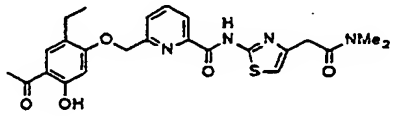
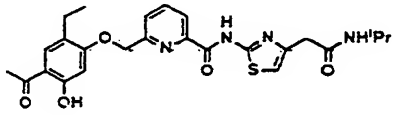
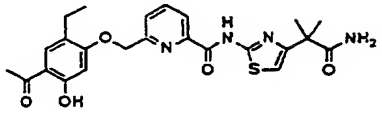
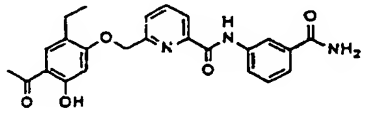
6	
7	
8	
9	
10	

Table 55

	^{1}H-NMR δppm
6	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 2.84(3H,d,J = 5.0Hz), 3.67(2H,s), 5.33(2H,s), 6.45(1H,s), 6.48(1H,bs), 6.85(1H,s), 7.51(1H,s), 7.74(1H,d,J = 6.6Hz), 8.02(1H,t,J = 6.6Hz), 8.27(1H,d,J = 6.6Hz), 11.06(1H,bs), 12.70(1H,s)
7	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.01(3H,s), 3.11(1H,s), 3.83(2H,s), 5.28(2H,s), 6.43(1H,s), 6.86(1H,b), 7.51(1H,s), 7.72(1H,dd,J = 1.0Hz,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,dd,J = 1.0Hz,J = 7.9Hz), 11.08(1H,bs), 12.70(1H,s)
8	(solvent:$CDCl_3$) 1.15(6H,d,J = 6.6Hz), 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.63(2H,s), 4.0-4.2(1H,m), 5.32(1H,s), 6.06(1H,bs), 6.45(1H,s), 6.85(1H,s), 7.51(1H,s), 7.74(1H,d,J = 7.9Hz), 8.02(1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 11.06(1H,bs), 12.70(1H,s)
9	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.31(3H,s), 1.34(3H,s), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.1-3.2(1H,m), 5.30(2H, s), 6.44(1H,s), 6.62(1H,s), 7.51(1H,s), 7.71(1H,d,J = 7.9Hz), 7.99(1H,dd,J = 6.6Hz,J = 7.9Hz), 8.26(1H,d,J = 6.6Hz), 11.05(1H,bs), 12.67(1H,s)
10	(solvent:$CDCl_3$) 1.23(3H,t,J = 7.6Hz), 2.60(3H,s), 2.65(2H,q,J = 7.6Hz), 5.49(2H,s), 6.64(1H,s), 7.35-7.55(2H,m), 7.6-7.8(3H,m), 8.0-8.3(5H,m), 10.59(1H,bs), 12.60(1H,s)

Table 56

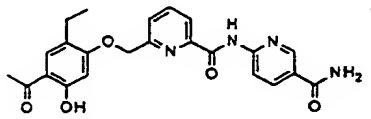
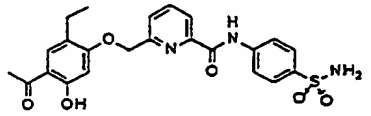
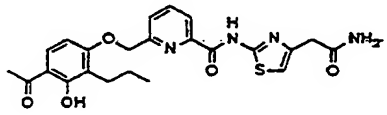
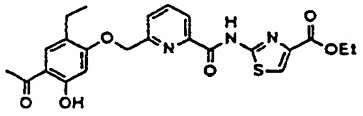
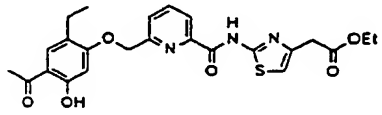
Ex. No.	Structural formula
11	
12	
13	
14	
15	

Table 57

	^{1}H-NMR	δppm
11	(solvent:$CDCL_3$) 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 5.49(1H,s), 6.64(1H,s), 7.53(1H,bs), 7.71(1H,s), 7.80-7.85(1H,m), 8.1-8.4(5H,m), 8.85-8.90(1H,m), 10.63(1H,bs), 12.56(1H,s)	
12	(solvent:$CDCL_3$) 1.20(3H,t,J = 7.6Hz), 2.58(2H,s), 2.64(2H,q,J = 7.6Hz), 5.47(2H,s), 6.62(1H,s), 7.30(2H,s), 7.71(1H,s), 7.75-7.90(3H,m), 8.0-8.2(4H,m), 10.75(1H,bs), 12.56(1H,s)	
13	(solvent:$CDCL_3$) 1.00(3H,t,J = 7.4Hz), 1.63(2H,tq,J = 7.4Hz,J = 7.4Hz), 2.58(3H,s), 2.77(2H,t,J = 7.4Hz), 3.69(2H,s), 5.36(2H,s), 5.40(1H,bs), 6.47(1H,d,J = 9.2Hz), 6.50(1H,bs), 6.87(1H,s), 7.62(1H,d, J = 9.2Hz), 7.76(1H,d,J = 7.9Hz, 8.02(1H,dd,J = 7.9Hz, J = 7.9Hz), 8.26(1H,d,J = 7.9Hz)	
14	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.43(3H,t,J = 7.1Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.45(2H,q,J = 7.1Hz), 5.28(1H,s) 6.43(1H,s), 7.52(1H,s), 7.73(1H,d,J = 7.9Hz), 7.94(1H,d,J = 0.7Hz) 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 11.32(1H,bs), 12.66(1H,s)	
15	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.30(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.76(2H,d,J = 0.7Hz), 4.22(2H,q,J = 7.3Hz), 5.28(1H,s), 6.43(1H,s), 6.90(1H,d,J = 0.7 Hz), 7.51(1H,s), 7.72(1H,d,J = 7.9Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.25(1H,d,J = 7.6Hz), 11.11(1H,bs), 12.67(1H,s)	

Table 58

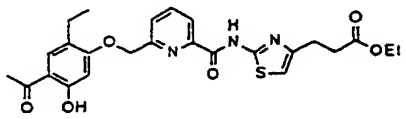
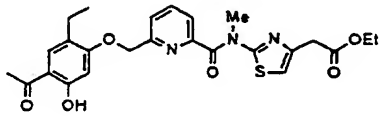
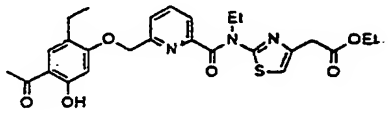
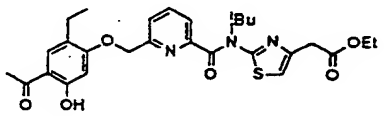
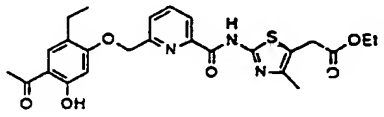
Ex. No.	Structural formula
16	
17	
18	
19	
20	

Table 59

	^{1}H-NMR δppm
16	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.65-2.80(4H,m), 3.05(2H,t,J = 7.3Hz), 4.15(2H,q,J = 7.3Hz), 5.30(2H,s), 6.44(1H,s), 6.69(1H,s), 7.51 (1H,s), 7.71(1H,d,J = 7.7Hz), 7.97(1H,t,J = 7.7Hz), 8.24(1H,d,J = 7.7Hz), 11.05(1H,bs), 12.67(1H,s)
17	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.43(3H,t,J = 7.1Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.45(2H,q,J = 7.1Hz), 5.28(1H,s) 6.43(1H,s), 7.52(1H,s), 7.73(1H,d,J = 7.9Hz), 7.94(1H,d,J = 0,7Hz) , 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 11.32(1H,bs), 12.66(1H,s)
18	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.1Hz), 1:40(3H,t,J = 6.9Hz), 2.58(3H,s),2.69(2H,q,J = 7.6Hz), 3.76(2H,d,J = 0.7Hz), 4.20(2H,q,J = 7.1Hz), 4.32(2H,q,J = 6.9Hz), 5.25(1H,s), 6.44(1H,s), 6.92(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.70(1H,d,J = 6.9Hz), 7.92(1H,dd,J = 6.9Hz,J = 7.6Hz), 12.65(1H,s)
19	(solvent:$CDCl_3$) 0.76(6H,d,J = 6.6Hz), 1.26(3H,t,J = 7.6Hz), 1.27(3H,t,J = 7.1Hz), 2.0-2.2(1H,m), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.74(2H,s), 4.18(2H,d,J = 7.1Hz), 4.28(2H,d,J = 6.9Hz), 5.21(2H,s), 6.43(1H,s), 6.91(1H,s), 7.49(1H,s), 7.58(1H,d,J = 7.9Hz), 7.71(1H,d,J = 7.9Hz), 7.90(1H,t,J = 7.9Hz), 12.63(1H,s)
20	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 1.29(3H,t,J = 7.3Hz), 2.33(3H,s), 2.59(3H,s), 2.69(2H,q,J = 7.4Hz), 3.73(2H,s), 4.20(2H,q,J = 7.3Hz), 5.27(2H,s), 6.43(1H,s), 7.51(1H,s), 7.71(1H,d,J = 7.9Hz), 7.99(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 10.98(1H,bs), 12.67(1H,s)

Table 60

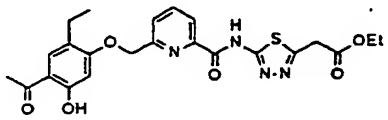
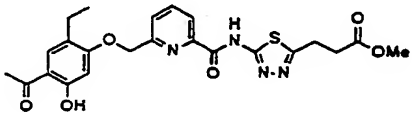
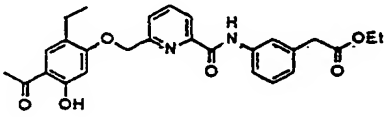
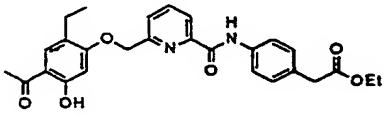
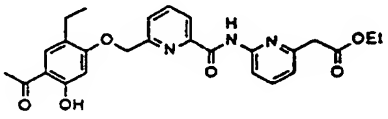
Ex. No.	Structural formula
21	
22	
23	
24	
25	

Table 61

	^{1}H-NMR	δppm
21	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz). 1.32(3H,t,J = 7.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.1Hz), 4.16(2H,s), 4.27(2H,q,J = 7.6Hz) 5.32(2H,s), 6.44(1H,s), 7.52(1H,s), 7.75(1H,d,J = 7.6Hz), 8.02(1H,t,J = 7.6Hz), 8.26(1H,d,J = 7.6Hz), 11.21(1H,bs), 12.67(1H,s)	
22	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2.70(2H,q,J = 7.4Hz), 2.93(2H,t,J = 7.3Hz), 3.40(2H,t,J = 7.3Hz), 3.73(3H,s), 5.32(2H,s), 6.43(1H,s), 7.51(1H,s), 7.75(1H,d,J = 7.9Hz), 8.01(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 11.18(1H,bs), 12.66(1H,s)	
23	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.66(2H,s), 4.17(2H,q,J = 7.3Hz) 5.32(2H,s), 6.52(1H,s), 7.0-7.1(1H,m), 7.3-7.4(1H,m), 7.51(1H,s), 7.65-7.7(2H,m), 7.97(1H,t,J = 7.7Hz), 8.26(1H,dd,J = 1.0Hz,J = 7.7Hz), 9.92(1H,bs), 12.68(1H,s)	
24	(solvent:$CDCL_3$) 1.26(3H,t,J = 7.1Hz), 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.62(2H,s), 4.16(2H,q,J = 7.1Hz) 5.32(2H,s), 6.51(1H,s), 7.32(1H,d,J = 8.6Hz), 7.51(1H,s), 7.67(1H,d,J = 7.3Hz), 7.75(1H,d,J = 8.6Hz), 7.98(1H,dd,J = 7.3Hz,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 9.90(1H,bs), 12.68(1H,s)	
25	(solvent:$CDCL_3$) 1.28(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.80(2H,s), 4.21(2H,q,J = 7.3Hz) 5.34(2H,s), 6.47(1H,s), 7.09(1H,d,J = 6.9Hz), 7.51(1H,s), 7.65-7.85(2H,m), 7.97(1H,t,J = 7.6Hz), 8.26(1H,t,J = 7.6Hz), 8.30(1H,t,J = 7.6Hz), 10.37(1H,bs), 12.66(1H,s)	

Table 62

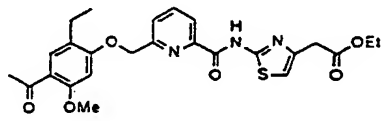
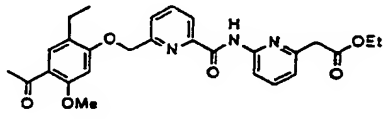
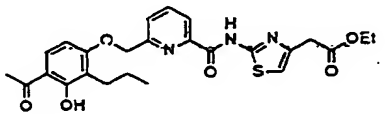
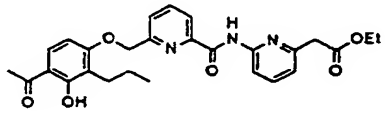
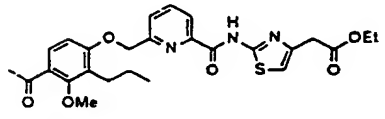
Ex. No.	Structural formula
26	
27	
28	
29	
30	

Table 63

	^{1}H-NMR δppm
26	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.3Hz), 1.30(3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.5Hz), 3.77(2H,s), 3.92(2H,s), 4.22(2H,q,J = 7.5Hz), 5.32(2H,s), 6.50(1H,s), 6.91(1H,s), 7.73(1H,s), 7.80(1H,d,J = 7.6Hz), 8.03(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.24(1H,d,J = 7.6Hz), 11.18(1H,s)
27	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.4Hz), 2.59(3H,s), 2.72(2H,q,J = 7.5Hz), 3.80(2H,s), 3.92(3H,s), 4.21(2H,q,J = 7.5Hz), 5.38(2H,s), 6.57(1H,s), 7.10(1H,dd,J = 7.0Hz ,J = 0.7Hz), 7.73(1H,s), 7.76(1H,dd,J = 8.3Hz, J = 7.9Hz), 7.77(1H,dd ,J = 7.9Hz,J = 1.0Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(1H,dd, J = 7.9Hz,J = 1.0Hz), 8.37(1H,d,J = 8.3Hz), 10.40(1H,s)
28	(solvent:$CDCl_3$) 1.00(3H,t,J = 7.4Hz), 1.30(3H,t,J = 7.1Hz), 1.63 (2H,tq, J = 7.9Hz, J = 7.3Hz), 2.58(3H,s), 2.77(2H,t,J = 7.6Hz), 3.77(2H,s), 4.22(2H,q,J = 7.0Hz), 5.32(1H,s), 6.46(1H,d,J = 8.9Hz) 6.91(1H,s), 7.62(1H,d,J = 8.9Hz), 7.74(1H,d,J = 7.9Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.24(1H,dd,J = 7.6Hz, J = 0.6Hz)
29	(solvent:$CDCl_3$) 1.00(3H,t,J = 7.4Hz), 1.29(3H,t,J = 7.2Hz), 1.64 (2H,tq,J = 7.6Hz,J = 7.2Hz), 2.58(3H,s), 2.78(2H,t,J = 7.2Hz), 3.81 (2H,s), 4.21(2H,q,J = 7.0Hz), 5.38(2H,s), 6.50(1H,d,J = 8.9Hz), 7.10(1H,dd,J = 7.3Hz,J = 0.7Hz), 7.62(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.9Hz), 7.76(1H,dd,J = 8.0Hz,J = 7.9Hz), 7.97(1H,dd,J = 7.9Hz, J = 7.6Hz), 8.25(1H,d,J = 6.9Hz), 8.36(1H,d,J = 7.6Hz)
30	(solvent:$CDCl_3$) 1.03(3H,t,J = 7.3Hz), 1.64(2H,tq,J = 7.6Hz,J = 7.8Hz), 2.59(3H,s), 2.74(2H,t,J = 8.0Hz), 3.78(3H,s), 3.82(2H,s), 5.31(2H,s), 6.71(1H,d,J = 8.9Hz), 6.83(1H,s), 7.53(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.19(1H,d,J = 7.6Hz)

Table 64

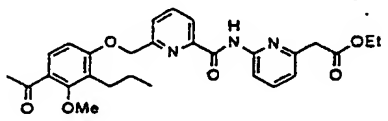
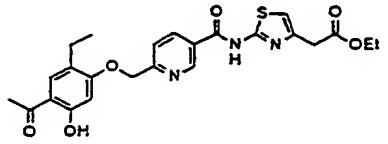
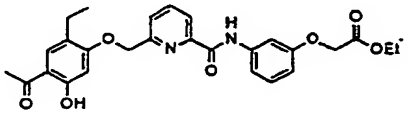
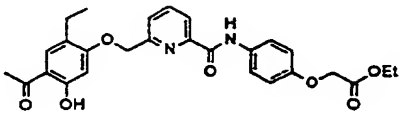
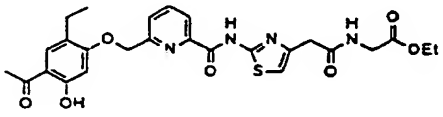
Ex. No.	Structural formula
31	
32	
33	
34	
35	

Table 65

	^{1}H-NMR	δppm
31	(solvent:$CDCL_3$) 1.03(3H,t,J = 7.3Hz), 1.65(2H,tq,J = 7.6Hz,J = 7.9Hz), 2.63(3H,s), 2.76(2H,t,J = 7.6Hz), 3.79(3H,s), 3.90(2H,s), 5.3 7(2H,s), 6.81(1H,d,J = 8.6Hz), 7.06(1H,d,J = 7.6Hz), 7.59(1H,d,J = 8 .9Hz), 7.75(1H,d,J = 6.9Hz), 7.83(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.01(1 H,dd,J = 7.9Hz,J = 7.9Hz), 8.28(1H,d,J = 6.9Hz), 8.37(1H,d,J = 7.9Hz)	
32	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.72(2H,s), 4.17(2H,q,J = 7.3Hz) 5.32(2H,s), 6.43(1H,s), 6.89(1H,s), 7.51(1H,s), 7.67(1H,dd,J = 0.7Hz,J = 8.2Hz), 8.29(1H,dd,J = 2.3Hz,J = 8.2Hz), 9.14(1H,dd,J = 0.7Hz,J = 2.3Hz), 9.58(1H,bs), 12.66(1H,s)	
33	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.30(2H,q,J = 7.3Hz), 4.68(2H,s) 5.32(2H,s), 6.51(1H,s), 6.70-6.80(1H,m), 7.25-7.35(2H,m) 7.51(1H,s), 7.55-7.65(1H,m), 7.68(1H,d,J = 7.6Hz), 7.98(1H,dd,J = 6.6Hz,J = 7.6Hz), 8.26(1H,d,J = 6.6Hz), 9.90(1H,bs), 12.67(1H,s)	
34	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.31(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 4.26(2H,q,J = 7.3Hz), 4.63(2H,s) 5.31(2H,s), 6.51(1H,s), 6.96(2H,d,J = 9.1Hz), 7.51(1H,s), 7.66(1H,d,J = 8.6Hz), 7.71(2H,d,J = 9.1Hz), 7.97(1H,dd,J = 7.6Hz,J = 8.6Hz), 8.26(1H,d,J = 7.6Hz), 9.82(1H,s), 12.67(1H,s)	
35	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.73(2H,s), 4.07(2H,d,J = 5.3Hz) 4.20(2H,q,J = 7.3Hz), 5.32(2H,s), 6.45(1H,s), 6.88(1H,s), 7.03(1H,b), 7.51(1H,s), 7.74(1H,dd,J = 1.0Hz, J = 7.6Hz), 8.01(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.25(1H,dd,J = 1.0Hz,J = 7.9Hz), 11.08(1H,bs), 12.67(1H,s)	

Table 66

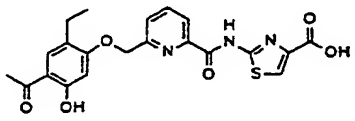
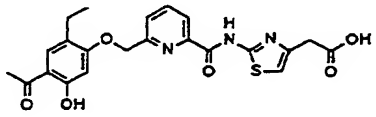
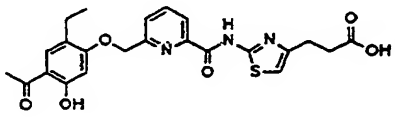
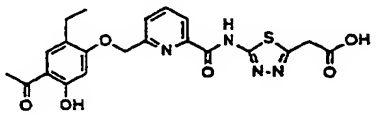
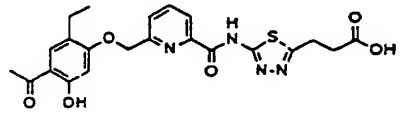
Ex. No.	Structural formula
36	
37	
38	
39	
40	

Table 67

	^{1}H-NMR	δppm
36	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.59(3H,s), 2.63(2H,q,J = 7.6Hz), 5.44(2H,s), 6.71(1H,s), 7.45(1H,s), 7.66,(1H,s), 7.7-7.8(1H,m), 8.10-8.20(2H,m), 12.60(1H,bs)	
37	(solvent:DMSO-d_6) 1.21(3H,t,J = 6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.67(2H,s), 5.46(2H,s), 6.63(1H,s), 7.11(1H,s), 7.70(1H,s), 7.78(1H,dd,J = 1.3Hz,J = 7.3Hz), 12.04(1H,bs), 12.55(1H,s)	
38	(solvent:DMSO-d_6) 1.21(3H,t,J = 7.4Hz), 2.59(3H,s), 2.55-2.75(4H,m), 2.89(2H,t,J = 7.6Hz), 5.47(2H,s), 6.63(1H,s), 6.95 (1H,s), 7.70(1H,s), 7.78(1H,d,J = 7.3Hz), 8.10-8.20(2H,m), 11.94(1H,bs), 12.57(1H,s)	
39	(solvent:DMSO-d_6) 1.21(3H,t,J = 7.4Hz), 2.58(3H,s), 2.65(2H,q,J = 7.4Hz), 4.15(2H,s), 5.47(2H,s), 6.63(1H,s), 7.70(1H,s), 7.80(1H,d,J = 6.9Hz), 8.10-8.20(2H,m), 12.50(1H,bs), 12.56(1H,s)	
40	(solvent:DMSO-d_6) 1.21(3H,t,J = 7.4Hz), 2.59(3H,s), 2.55-2.75(4H,m), 2.89(2H,t,J = 7.6Hz), 5.47(2H,s), 6.63(1H,s), 6.95(1H,s), 7.70(1H,s), 7.78(1H,d,J = 7.3Hz), 8.10-8.20 (2H,m), 11.94(1H,bs), 12.57(1H,s)	

Table 68

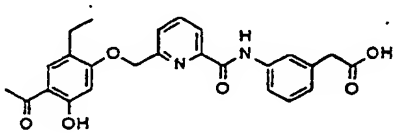
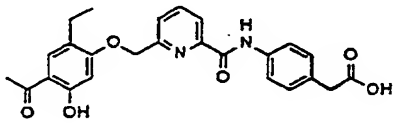
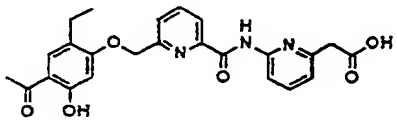
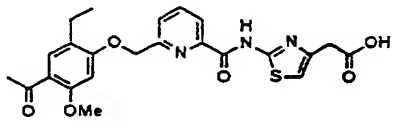
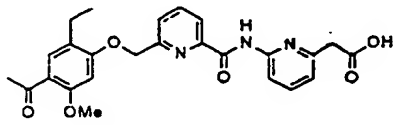
Ex. No.	Structural formula
41	
42	
43	
44	
45	

Table 69

	^{1}H-NMR	δppm
41	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.58(1H,s), 5.47(2H,s), 6.63(1H,s), 7.04(1H,d,J = 7.9Hz), 7.33(1H,m), 7.7-7.8(4H,m), 8.1-8.2(2H,m), 10.41(1H,s), 12.56(1H,s)	
42	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 5.46(2H,s), 6.62(1H,s), 7.27(2H,d,J = 8.2Hz) 7.65-7.85(4H,m), 8.05-8.20(2H,m), 8.10-8.20(2H,m), 10.40(1h,s) 12.56(1H,bs)	
43	(solvent:DMSO-d_6) 1.23(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.71(2H,s), 5.49(2H,s), 6.65(1H,s), 7.17(1H,d,J = 6.9Hz), 7.69(1H,s), 7.75-7.95(2H,m), 8.10-8.20 (3H,m), 10.33(1H,s), 12.55(1H,bs)	
44	(solvent:$CDCL_3$) 1.25(3H,t,J = 7.4Hz), 2.57(3H,s), 2.70(2H,q,J = 7.2Hz), 3.83(2H,s), 3.89(3H,s), 5.35(2H,s), 6.52(1H,s), 6.88(1H,s), 7.70(1H,s), 7.81(1H,d,J = 7.6Hz), 8.03(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.24(1H,d,J = 7.6Hz)	
45	(solvent:$CDCL_3$) 1.26(3H,t,J = 6.7Hz), 2.59(3H,s), 2.72(2H,q,J = 6.9Hz), 3.91(2H,s), 3.93(3H,s), 5.39(2H,s), 6.55(1H,s), 7.07(1H,d,J = 7.3Hz), 7.74(1H,s), 7.83(1H,d,J = 6.6Hz) 7.86(1H,dd,J = 7.8Hz,J = 7.6Hz), 8.04(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.29(1H,d,J = 6.6Hz), 8.41(1H,d,J = 8.3Hz)	

Table 70

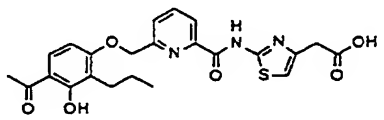
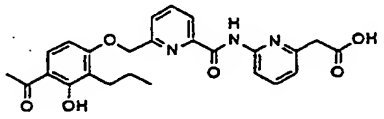
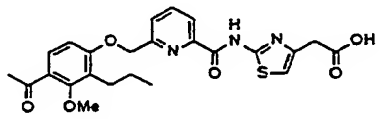
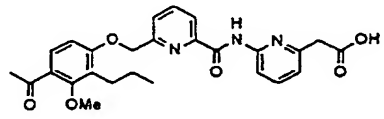
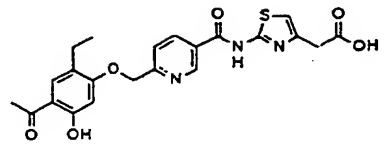
Ex. No.	Structural formula
46	
47	
48	
49	
50	

Table 71

	^{1}H-NMR	δppm
46	(solvent:DMSO-d_6) 0.92(3H,t,J = 7.3Hz), 1.55(2H,tq,J = 6.9Hz, J = 7.7Hz), 2.52(3H,s), 2.67(2H,t,J = 7.6Hz), 3.67(2H,s), 5.50(2H,s), 6.77(1H,d,J = 9.2Hz), 7.11(1H,s), 7.76(1H,d,J = 7.2Hz) 7.81(1H,d,J = 8.9Hz), 8.11(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.13(1H,d,J = 7.6Hz)	
47	(solvent:$CDCL_3$) 1.00(3H,t,J = 7.4Hz), 1.64(2H,tq,J = 7.6Hz, J = 7.3Hz), 2.59(3H,s), 2.78(2H,t,J = 7.6Hz), 3.91(2H,s), 5.40(2H,s), 6.55(1H,d,J = 8.9Hz), 7.07(1H,d,J = 6.6Hz), 7.63(1H,d,J = 8.2Hz), 7.77(1H,d,J = 6.9Hz), 7.85(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.02(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(H,d,J = 6.9Hz), 8.39(1H,d,J = 8.3Hz)	
48	(solvent:$CDCL_3$) 1.03(3H,t,J = 7.3Hz), 1.64(2H,tq,J = 7.6Hz,J = 7.8Hz), 2.59(3H,s), 2.74(2H,t,J = 8.0Hz), 3.78(3H,s), 3.82(2H,s) 5.31(2H,s), 6.71(1H,d,J = 8.9Hz), 6.83(1H,s), 7.53(1H,d,J = 8.9Hz), 7.70(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.19(1H,d,J = 7.6Hz)	
49	(solvent:$CDCL_3$) 1.03(3H,t,J = 7.3Hz), 1.65(2H,tq,J = 7.6Hz,J = 7.9Hz), 2.63(3H,s), 2.76(2H,t,J = 7.6Hz), 3.79(3H,s), 3.90(2H,s), 5.37(2H,s), 6.81(1H,d,J = 8.6Hz), 7.06(1H,d,J = 7.6Hz), 7.59(1H,d, J = 8.9Hz), 7.75(1H,d,J = 6.9Hz), 7.83(1H,dd,J = 7.9Hz, J = 7.9Hz), 8.01(1H,dd,J = 7.9Hz,J = 7.9Hz), 8.28(1H,d,J = 6.9Hz) 8.37(1H,d,J = 7.9Hz)	
50	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.66(2H,s), 5.38(2H,s), 6.57(1H,s), 7.06(1H,s), 7.66(1H,d,J = 8.6Hz), 7.69(1H,s), 8.48(1H,dd,J = 2.0Hz,J = 8.6Hz), 9.22(1H,d,J = 2.0Hz), 12.54(1H,s)	

Table 72

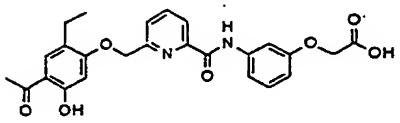
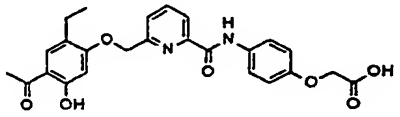
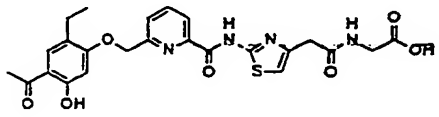
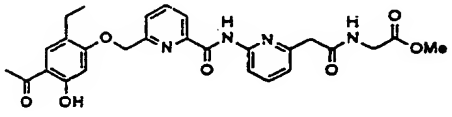
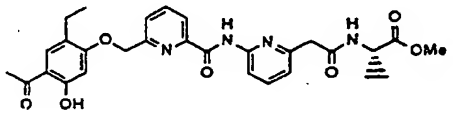
Ex. No.	Structural formula
51	
52	
53	
54	
55	

Table 73

	^{1}H-NMR δppm
51	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.64(2H,s), 5.45(2H,s), 6.62(1H,s), 6.93(2H,d,J = 8.2Hz), 7.65-7.85(4H,m), 8.05-8.20(2H,m), 10.35(1H,s), 12.55(1H,s)
52	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.66(2H,s), 5.46(2H,s), 6.62(1H,s), 6.65-6.75(1H,m), 7.20-7.80(5H,m), 8.05-8.20(2H,m), 10.41(1H,s) 12.56(1H,s),
58	(solvent:DMSO-d_6) 1.21(3H,t,J = 7.3Hz), 2.58(3H,s), 2.65(2H,q,J = 7.3Hz), 3.60(2H,s), 3.79(2H,d,J = 5.6Hz), 5.46(2H,s) 6.63(1H,s), 7.09(1H,s), 7.70(1H,s), 7.75-7.85(1H,m), 8.1-8.4(3H,m), 12.04(1H,bs), 12.56(1H,s)
54	(solvent:$CDCL_3$) 1.31(3H,t,J = 7.6Hz), 1.52(2H,d,J = 6.9Hz), 2.57(3H,s), 2.74(2H,q,J = 7.6Hz), 3.71(2H,s), 4.60(1H,dq,J = 7.6Hz,J = 7.9Hz), 5.49(2H,s), 6.84(1H,s), 7.01(1H,d,J = 7.3Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6Hz), 7.75(1H,dd,J = 7.6Hz,J = 8.2Hz), 7.93(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.22(1H,d,J = 7.9Hz), 8.33(1H,d,J = 8.3Hz)
55	(solvent:$CDCL_3$) 1.27(3H,t,J = 7.6Hz), 1.43(2H,d,J = 7.3Hz), 2.59(3H,s), 2.71(2H,q,J = 7.3Hz), 3.72(3H,s), 3.74(2H,s), 4.61(2H,dq,J = 6.9Hz,J = 7.2Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 7.6Hz), 7.51(1H,s), 7.72(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 7.2Hz,J = 3.4Hz), 8.00(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.34(1H,d,J = 8.6Hz)

Table 74

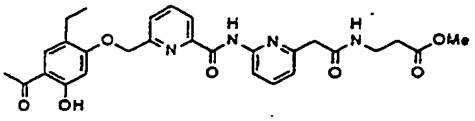
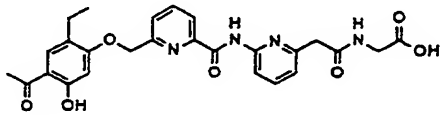
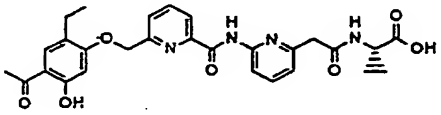
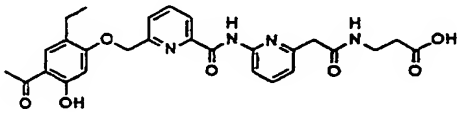
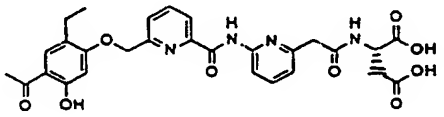
Ex. No.	Structural formula
56	
57	
58	
59	
60	

Table 75

	^{1}H-NMR δppm
56	(solvent:$CDCL_3$) 1.28(3H,t,J = 7.4Hz), 2.59(3H,s), 2.54(2H,t, J = 6.1Hz), 2.70(2H,t,J = 7.4Hz), 3.55(3H,s), 3.56(2H,dd,J = 5.9Hz, J = 6.3Hz), 3.69(2H,s), 5.39(2H,s), 6.50(1H,s), 7.06(1H,d, J = 7.6Hz), 7.51(1H,s), 7.73(1H,dd,J = 7.9Hz,J = 1.0Hz), 7.75(1H,dd, J = 7.6Hz,J = 7.9Hz), 7.99(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.30(1H,d, J = 7.9Hz, J = 1.0Hz), 8.32(1H,d,J = 8.3Hz)
57	(solvent:$CDCL_3$) 1.28(3H,t,J = 7.6Hz), 2.60(3H,s), 2.72(2H,q, J = 7.5Hz), 3.76(2H,s), 5.40(2H,s), 6.55(1H,s), 7.13(1H,d,J = 7.3Hz), 7.54(1H,s), 7.76(1H,dd,J = 7.3Hz, J = 7.6Hz), 7.81(1H,d,J = 7.6Hz), 8.02(1H,dd,J = 7.9Hz, J = 7.9Hz), 8.25(1H,d,J = 7.3Hz), 8.31(1H,d,J = 8.2Hz)
58	(solvent:$CDCL_3$) 1.31(3H,t,J = 7.6Hz), 1.52(2H,d,J = 6.9Hz), 2.57(3H,s), 2.74(2H,q,J = 7.6Hz), 3.71(2H,s), 4.60(1H,dq,J = 7.6Hz,J = 7.9Hz), 5.49(2H,s), 6.84(1H,s), 7.01(1H,d,J = 7.3Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6Hz), 7.75(1H,dd,J = 7.6Hz,J = 8.2Hz), 7.93(1H,dd,J = 7.6Hz,J = 7.6Hz), 8.22(1H,d,J = 7.9Hz), 8.33(1H,d,J = 8.3Hz)
59	(solvent:$CDCL_3$) 1.28(3H,t,J = 7.6Hz), 2.58(3H,s), 2.60(2H,q,J = 5.9Hz), 2.71(2H,q,J = 7.9Hz), 3.70(2H,s), 3.60(2H,q,J = 5.7Hz), 5.44(1H,s), 6.74(1H,s), 7.03(1H,d,J = 7.6Hz) 7.50(1H,s), 7.73(1H,d,J = 7.3Hz), 7.74(1H,dd,J = 8.5Hz,J = 7.3Hz), 8.00(1H,dd,J = 7.9Hz,J = 7.6Hz), 8.25(1H,d,J = 7.6Hz), 8.31(1H,d,J = 8.2Hz)
60	(solvent:$CDCL_3$) 1.29(3H,t,J = 7.6Hz), 2.60(3H,s), 2.73(2H,q, J = 7.5Hz), 2.85(1H,dd,J = 17.2Hz,J = 5.3Hz), 3.00(1H,dd,J = 14.2Hz,J = 4.6Hz), 3.76(2H,s), 4.78(1H,t,J = 5.0Hz), 5.41(2H,s), 6.55(1H,s) , 7.13(1H,d,J = 7.6Hz), 7.55(1H,s), 7.74(1H,d,J = 7.8Hz), 7.79(1H,dd,J = 7.6Hz,J = 8.2Hz), 8.02(1H,dd,J = 7.6Hz,J = 7.9Hz), 8.23(1H,d,J = 6.9Hz), 8.30(1H,d,J = 8.6Hz)

Table 76

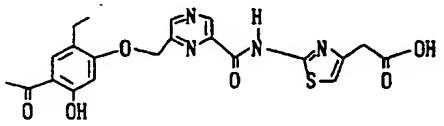
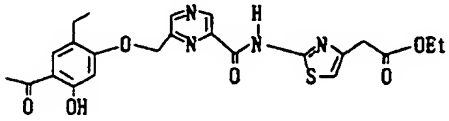
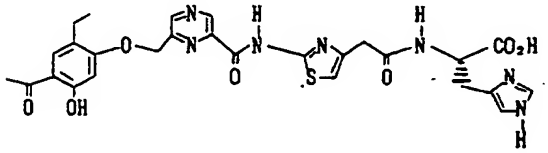
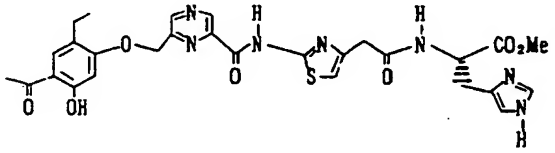
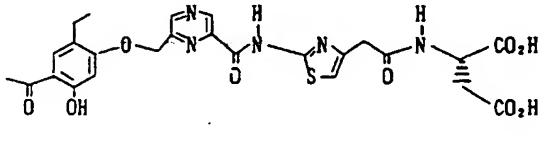
Ex. No.	Structural formula
61	
62	
63	
64	
65	

Table 77

	^{1}H-NMR	δppm
61	(solvent:DMSO-d_6) 1.19(3H,t,J=7.6Hz), 2.59(3H,s), 2.64(2H,q,J= 7,6Hz), 3.67(2H,s), 5.49(2H,s), 6.69(1H,s), 7,12(1H,s), 7,71 (1H,s), 9,04(1H,s), 9.27(1H,s), 10.06(1H,s), 12.58(1H,br)	
62	(solvent:$CDCL_3$) 1.26(3H,t,J=7.6Hz), 1.30(3H,t,J=7.3Hz), 2.60 (3H,s), 2.69(2H,q,J=7,6Hz), 3.76(2H,d,J=0.7Hz), 4.22(2H,q,J= 7.3Hz), 5.33(2H,s), 6.47(1H,s), 6.94(1H,s), 7.53(1H,s), 9.08 (1H,s), 9.48(1H,s), 10.90(1H, br), 12.70(1H,s)	
63	(solvent:DMSO-d_6) 1.19(3H,t,J=7,6Hz), 2.59(3H,s), 2.66(2H,q,J= 7,6Hz), 2.89(1H,dd,J=8.3Hz,15.0Hz), 3.00(1H,dd,J=5.3Hz,15.0 Hz), 3.58(2H,s), 4.4-4.5(1H,m), 5.49(2H,s), 6.68(1H,s), 6.94 (1H,s), 7.00(1H,s), 7.71(1H,s), 7.87(1H,s), 8.33(1H,d,J=7.6 Hz), 9.05(1H,s), 9.27(1H,s), 12.60(1H,br)	
64	(solvent:$CDCl_3$) 1.20(3H,t,J=7.3Hz), 2.60(3H,s), 2.70(2H,q,J= 7.3Hz), 3.1-3.2(2H,m), 3.72(3H,s), 3.75(2H,s), 4.8-4.9(1H,m), 5.36(2H,s), 6.48(1H,s), 6.79(1H,s), 6.91(1H,s), 7.53(1H,s), 7.56(1H,s), 9.10(1H,s), 9.48(1H,s), 12.78(1H,br)	
65	(solvent:DMSO-d_6) 1.19(3H,t,J=7.6Hz), 2.59(3H,s), 2.6-2.7(4H, m),3.61(2H,s), 4.5-4.6(1H,m), 5.49(2H,s), 6.69(1H,s), 7.08(1H, s), 8.35(1H,d,J=7.6Hz), 9.05(1H,s), 9.27(1H,s), 12.60(1H,s),	

Table 78

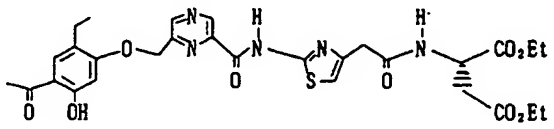
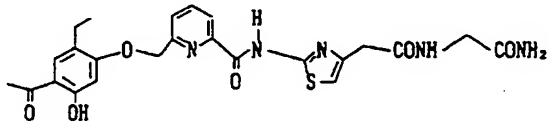
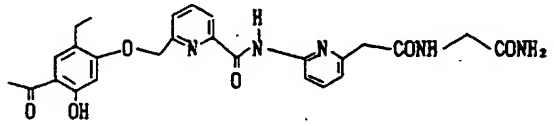
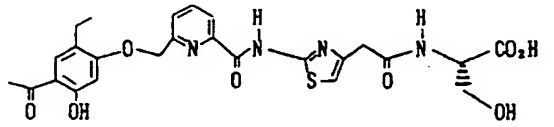
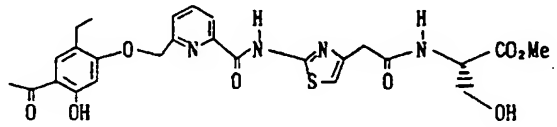
Ex. No.	Structural formula
66	
67	
68	
69	
70	

Table 79

	^{1}H-NMR	δppm
66	(solvent:$CDCl_3$) 1.16(3H,t,J = 7.6Hz), 1.25(3H,t,J = 7.6Hz), 1.26 (3H,t,J = 7.6Hz), 2.59(3H,s), 2.69(2H,q,J = 7.6Hz), 2.8-3.1(2H,m), 3.71(2H,s), 4.11(2H,q,J = 7.6Hz), 4.21(2H,q,J = 7.6Hz), 4.8-4.9 1H,m), 5.37(2H,s), 6.47(1H,s), 6.91(1H,s), 7.52(1H,s), 8.03 (1H,s), 9.08(1H,s), 9.49(1H,s), 12.68(1H,s),	
67	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.59(3H,t), 2.70(2H,q,J = 7.6Hz), 3.76(2H,s), 3.78(2H,d,J = 0.7Hz), 5.28(2H,s), 6.43(1H, s), 7.51(1H,s), 6.90(1H,s), 7.72(1H,dd,J = 7.9, 1.0Hz), 8.00(1H, dd,J = 7.9, 7.6Hz), 8.25(1H,d,J = 7.9Hz)	
68	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 2.58(3H,s), 2.72(2H,q,J = 7.5Hz), 3.77(2H,s), 4.05(2H,d,J = 5.0Hz), 5.46(2H,s), 6.89(1H, s), 7.03(1H,d,J = 6.6Hz), 7.5(1H,s), 7.72(1H,d,J = 7.9Hz), 7.76 (1H,dd,J = 7.6, 7.9Hz), 7.99(1H,dd,J = 7.6, 7.9Hz), 8.24(1H,d,J = 7.6Hz), 8.30(1H,d,J = 8.3Hz)	
69	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.72(2H,s), 3.8-4.0(2H,m), 4.58(3H,t,J = 3.8Hz), 5.33 (2H,s), 6.48(1H,s), 6.94(1H,s), 7.52(1H,s), 7.76(1H,d,J = 7.6 Hz), 8.03(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.9Hz)	
70	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.60(3H,s), 2.71(2H,q,J = 7.5Hz), 3.37(2H,s), 3.73(3H,s), 3.87(1H,dd,J = 11.5, 3,3Hz), 3.97 (1H,dd,11.5, 3,3Hz), 4.6-4.7(1H,m), 5.34(2H,s), 6.48(1H, s), 6.96(1H,s), 7.54(1H,s), 7.77(1H,d,J = 7.6Hz), 8.04(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.6Hz)	

Table 80

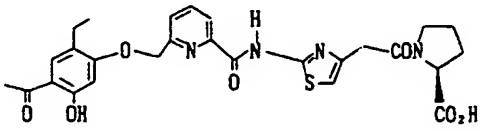
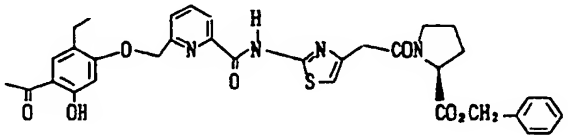
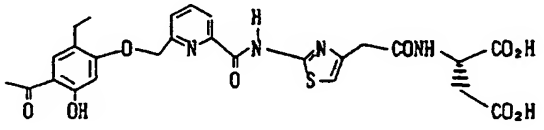
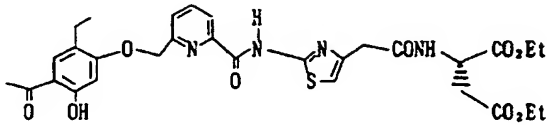
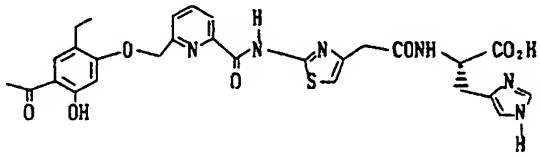
Ex. No.	Structural formula
71	
72	
73	
74	
75	

Table 81

	^{1}H-NMR δppm
71	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.5-2.2(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.6Hz), 3.5-3.7(2H,m), 3.85(2H,d,J = 2.3Hz), 4.6-4.7 (1H,m), 5.32(2H,s), 6.49(1H,s), 6.92(1H,s), 7.51(1H,s), 7.73 (1H,d,J = 7.9Hz), 7.99(1H,dd,J = 7.9, 7.9Hz), 8.23(1H,d,J = 7.9Hz)
72	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.5Hz), 3.6-3.8(2H,m), 3.82(2H,s), 4.12(2H,q,J = 7.2Hz), 4.63(1H,dd,J = 8.3, 3.6Hz), 5.18(2H,d,J = 7.9Hz), 5.27(2H, s), 6.44(1H,s), 6.94(1H,s), 7.35(5H,m), 7.51(1H,s), 7.72(1H,d, J = 6.9Hz), 8.00(1H,dd,J = 7.9, 7.9Hz), 8.25(1H,d,J = 7.9Hz)
73	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.60(3H,s), 2.71(2H,q,J = 7.3Hz), 2.8-3.1(2H,m), 3.37(2H,d,J = 5.0Hz), 3.71(2H,s), 4.80 (1H,t,J = 4.8Hz), 5.35(2H,s), 6.49(1H,s), 6.93(1H,s), 7.54(1H, s), 7.76(1H,d,J = 7.9Hz), 8.03(1H,dd,J = 7.9, 7.9Hz), 8.23(1H,d,J = 7.9Hz)
74	(solvent:$CDCl_3$) 1.19(3H,t,J = 7.1Hz), 1.24(3H,t,J = 7.4Hz), 1.27 (3H,t,J = 7.8Hz), 2.59(3H,s), 2.70(2H,q,J = 7.2Hz), 2.85(1H,dd,J = 17.2. 4.6Hz), 3.02(1H,dd,J = 16.8, 4.6Hz), 3.72(2H,s), 4.10(2H, q,J = 7.2Hz), 4.20(2H,q,J = 7.1Hz), 4.85(1H,td, J = 4.9, 7.6Hz), 5.31(2H,s), 6.44(1H,s), 6.89(1H,s), 7.51(1H,s), 7.74(1H,d,J = 7.6Hz), 8.01(1H,dd,J = 7.6, 7.9Hz), 8.26(1H,d,J = 7.6Hz)
75	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.5Hz), 2.59(3H,s), 2.69(2H,q,J = 7.3Hz), 3.26(2H,d,J = 5.0Hz), 3.70(2H,s), 4.70(1H,t,J = 5.0Hz), 5.33(2H,s), 6.48(1H,s), 6.95(1H,s), 7.05(1H,s), 7.50(1H,s), 7.76(1H,d,J = 8.0Hz), 8.00(1H,dd,J = 8.0, 8.0Hz), 8.22(1H,d,J = 8.0 Hz)

Table 82

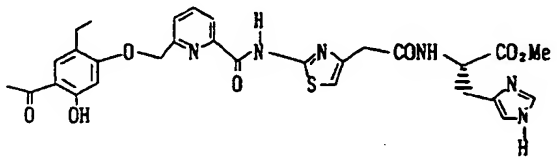
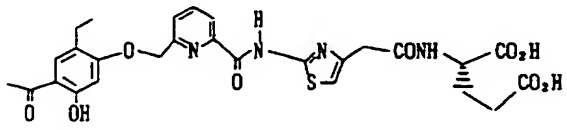
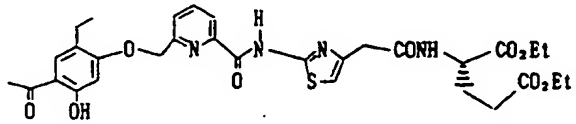
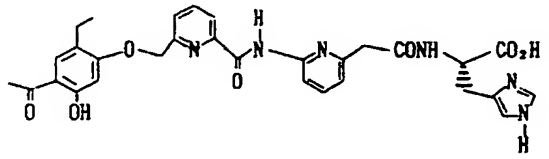
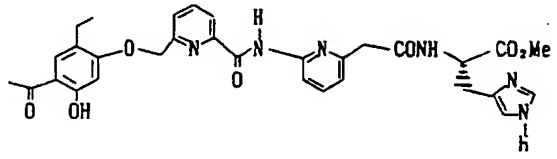
Ex. No.	Structural formula
76	
77	
78	
79	
80	

Table 83

	^{1}H-NMR	δppm
76	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.5Hz), 2.59(3H,s), 2.69(2H,q,J = 7.5Hz), 3.15(2H,t,J = 4.2Hz), 3.71(3H,s), 3.73(2H,s), 4.84(1H, dt, J = 7.3, 4.2Hz), 5.31(2H,s), 6.45(1H,s), 6.78(1H,s), 6.88(1H, s), 7.50(1H,s), 7.59(1H,s), 7.72(1H,d,J = 7.6Hz), 8.01(1H,dd,J = 7.9, 7.9Hz), 8.26(1H,d,J = 7.6Hz),	
77	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.5Hz), 1.9-2.5(4H,m), 2.0-2.5(4H, m), 2.60(3H,s), 2.71(2H,q,J = 7.5Hz), 3.70(2H,s), 4.56(1H,t,J = 4.0Hz), 5.35(2H,s), 6.49(1H,s), 6.94(1H,s), 7.36(1H,s), 7.77 (1H,d,J = 7.9Hz), 8.04(1H,dd,J = 7.6, 7.9Hz), 8.24(1H,d,J = 7.6Hz)	
78	(solvent:$CDCl_3$) 1.21(3H,t,J = 7.1Hz), 1.26(3H,t,J = 7.4Hz), 1.29 (3H,t,J = 7.6Hz), 1.9-2.4(4H,m), 2.59(3H,s), 2.70(2H,q,J = 7.4Hz), 3.70(2H,s), 4.09(2H,q,J = 7.2Hz), 4.19(2H,q,J = 6.9Hz), 4.63(1H, td,J = 3.7, 7.6Hz), 5.33(2H,s), 6.47(1H,s), 6.88(1H,s), 7.51(1H, s), 7.75(1H,d,J = 6.9Hz), 8.02(1H,dd,J = 6.9, 7.6Hz), 8.26(1H,d,J = 6.9Hz)	
79	(solvent:$CDCl_3$) 1.21(3H,t,J = 7.6Hz), 2.51(3H,s), 2.62(2H,q,J = 7.6Hz), 3.20(2H,br), 4.71(1H,t,J = 5.3Hz), 5.23(2H,s), 6.43(1H, s), 7.41(1H,s), 7.05(1H,s), 7.05(1H,d,J = 7.3Hz), 7.31(1H,s), 7.61(1H,dd,J = 7.9Hz), 7.67(1H,dd,J = 7.9, 7.9Hz), 7.90(1H,dd,J = 7.6, 7.6Hz), 8.12(1H,d,J = 7.3Hz), 8.19(1H,d,J = 8.3Hz),	
80	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.70(2H,q,J = 7.4Hz), 3.17(2H,d,J = 5.0Hz), 3.67(3H,s), 3.77(2H,s), 4.82(1H, dt,J = 6.9, 5.0 Hz), 5.22(2H,s), 6.35(1H,s), 6.71(1H,s), 7.07 (1H,d,J = 7.3Hz), 7.45(1H,s), 7.51(1H,s), 7.67(1H,d,J = 7.3Hz), 7.76(1H,dd,J = 7.9, 7.9Hz), 7.98(1H,dd,J = 7.9, 7.9Hz), 8.26(1H,d, J = 6.9Hz), 8.32(1H,d,J = 7.9Hz)	

Table 84

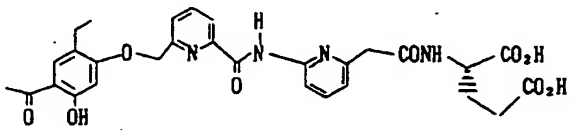
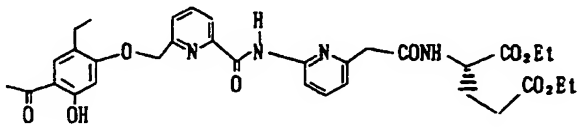
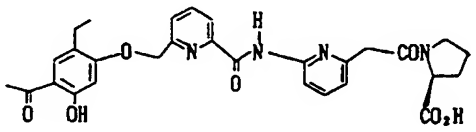
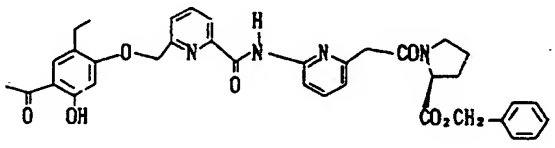
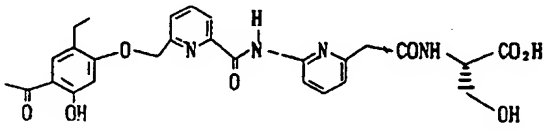
Ex. No.	Structural formula
81	
82	
83	
84	
85	

Table 85

	^{1}H-NMR δppm
81	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 1.9-2.5(4H,m), 2.60(3H,s), 2.72(2H,q,J = 7.4Hz), 3.84(2H,s), 4.5-4.6(1H,m), 5.42(2H,s), 6.56(2H,s), 7.26(1H,d,J = 7.9Hz), 7.54(1H,s), 7.76(1H,d,J = 8.3 Hz, 7.94(1H,dd,J = 7.9, 7.9Hz), 8.03(1H,dd,J = 7.9, 7.6Hz), 8.24 (1H,d,J = 7.9Hz), 8.39(1H,d,J = 8.6Hz)
82	(solvent:$CDCl_3$) 1.16(3H,t,J = 7.3Hz), 1.20(3H,t,J = 7.1Hz), 1.27 (3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz),2.0-2.4(4H,m), 3.74(2H,s), 4.03(2H,q,J = 7.1Hz), 4.1-4.3(2H,m), 4.65(1H,t,d,J = 7.6, 5.3Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 6.6Hz), 7.51 (1H,s), 7.71(1H,d,J = 7.3Hz), 7.73(1H,dd,J = 7.9, 7.9Hz), 7.99(1H, dd,J = 7.6, 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.34(1H,d,J = 7.9Hz)
83	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.0-2.1(4H,m), 2.58(3H,s), 2.71(2H,q,J = 7.4Hz), 3.67(2H,m), 3.94(2H,d,J = 4.3Hz), 4.75(1H, d,J = 5.9Hz), 5.39(2H,s), 6.56(2H,s), 7.10(1H,d,J = 7.6Hz), 7.50 (1H,s), 7.71(1H,d,J = 7.9Hz), 7.78(1H,dd,J = 7.9, 7.9Hz), 7.98(1H, dd, J = 7.9, 7.6Hz), 8.24(1H,d,J = 7.6Hz), 8.37(1H,d,J = 8.3Hz)
84	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.70(2H,q,J = 7.5Hz), 3.6-3.8(2H,m), 3.88(2H,s), 4.12(2H,q,J = 7.2 Hz), 4.63(1H,dd,J = 8.3, 3.6Hz), 5.17(2H,d,J = 7.9Hz), 5.31(2H,s), 6.47(1H,s), 7.15(1H,d,J = 6.6Hz), 7.34(5H,m), 7.50(1H,s), 7.67 (1H,d,J = 7.6Hz), 7.68(1H,dd,J = 7.9, 7.6Hz), 7.97(1H,dd,J = 7.9, 7.6Hz), 8.26(1H,d,J = 6.9Hz), 8.30(1H,d,J = 8.3Hz)
85	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 2.60(3H,s), 2.72(2H,q,J = 7.4Hz), 3.79(2H,s), 3.8-4.1(2H,m), 4.59(1H,t,J = 3.5Hz), 5.39 (2H,s), 6.52(1H,s), 7.54(1H,s), 7.74(1H,d,J = 7.9Hz), 7.80(1H, dd,J = 7.6, 8.3Hz), 8.02(1H,dd,J = 7.9, 7.6Hz), 8.24(1H,d,J = 7.9 Hz), 8.31(1H,d,J = 8.2Hz), 7.15(1H,d,J = 7.3Hz)

Table 86

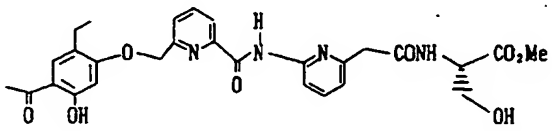
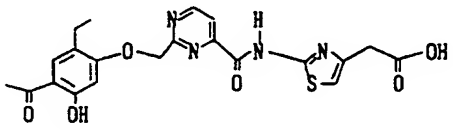
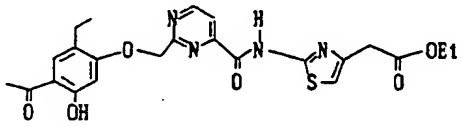
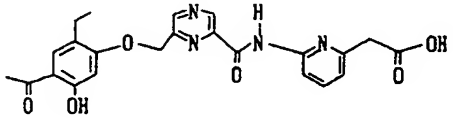
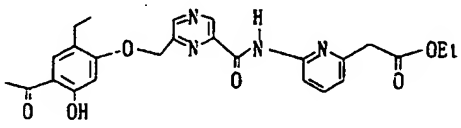
Ex. No.	Structural formula
86	
87	
88	
89	
90	

Table 87

	^{1}H-NMR	δppm
86	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2,69(2H,q,J = 7.4Hz), 3.74(3H,s), 3.79(2H,s), 4.00(2H,d,J = 3.3Hz), 4.71(1H, dt,J = 7.3, 3.6Hz), 5.38(2H,s), 6.50(1H,s), 7.05(1H,d,J = 6.6Hz), 7.49(1H,s), 7.70(1H,d,J = 7.9Hz), 7.75(1H,dd,J = 7.6, 8.2Hz), 7.98 (1H,dd,J = 7.9, 6.7Hz), 8.25(1H,d,J = 6.6Hz), 8.27(1H,d,J = 8.2Hz)	
87	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.60(3H,s), 2.64(2H,q,J = 7.6Hz), 3.53(2H,s), 5.49(2H,s), 6.55(1H,s), 6.89(1H,s), 7.64 (1H,s), 8.04(1H,d,J = 5.0Hz), 9.05(1H,s) (DMSO-d_5)	
88	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.58 (3H,s), 2.71(2H,q,J = 7.6Hz), 3.76(2H,s), 4.21(2H,q,J = 7.3Hz), 5.43(2H,s), 6.41(1H,s), 6.94(1H,s), 7.51(1H,s), 8.13(1H,d,J = 5.0Hz), 9.09(1H,d,J = 5.0Hz), 10.93(br), 12.64(1H,s)	
89	(solvent:DMSO-d_6) 1.22(3H,t,J = 7.6Hz), 2.59(2H,s), 2.67(2H,q, J = 7.6Hz), 3.73(2H,s), 5.56(2H,s), 6.71(1H,s), 7.20(1H,d,J = 7.6 Hz), 7.71(1H,s), 7.89(1H,dd,J = 7.6Hz,7.9Hz), 8.16(1H,d,J = 7.9 Hz), 9.08(1H,s), 9.32(1H,s), 10.22(1H,s), 12.58(1H,s)	
90	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.3Hz), 2.60 (3H,s), 2.70(2H,q,J = 7.6Hz), 3.80(2H,s), 4.21(2H,q,J = 7.3Hz), 5.38(2H,s), 6.50(1H,s), 7.12(1H,dd,J = 0.7Hz,7.6Hz), 7.52(1H,s), 7.78(1H,t,J = 7.9Hz), 8.34(1H,d,J = 8.3Hz), 9.04(1H,s), 10.06(1H, s), 12.68(1H,s)	

Table 88

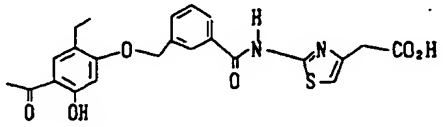
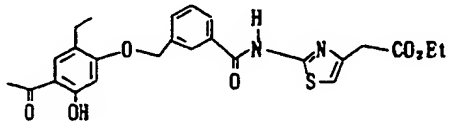
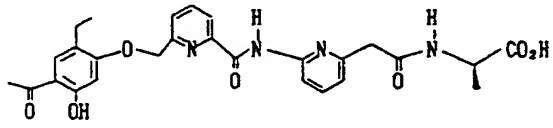
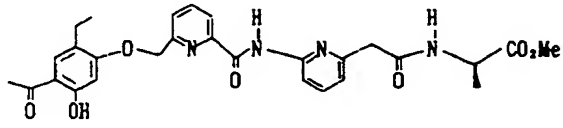
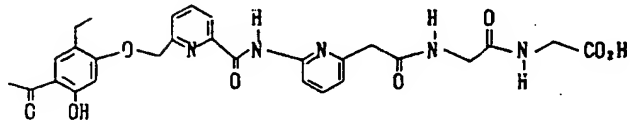
Ex. No.	Structural formula
91	
92	
93	
94	
95	

Table 89

	^{1}H-NMR	δppm
91	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.72(2H,s), 5.20(2H,s), 6.47(1H,s), 6.87(1H,s), 7.50 (1H,s), 7.58(1H,dd,J = 7.6, 7.6Hz), 7.69(1H,d,J = 7.6Hz), 7.98(1H, d,J = 7.6Hz), 8.09(1H,s)	
92	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.4Hz), 1.28(3H,t,J = 7.1Hz), 2.58 (3H,s), 2.64(2H,q,J = 7.4Hz), 3.69(2H,s), 4.19(2H,q,J = 7.1Hz), 5.18(2H,s), 6.45(1H,s), 6.86(1H,s), 7.47(1H,s), 7.57(1H,dd,J = 7.6, 7.6Hz), 7.68(1H,d,J = 7.6Hz), 7.88(1H,d,J = 7.6Hz), 8.02(1H, s)	
93	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.6Hz), 1.47(3H,d,J = 7.3Hz), 2.60 (3H,s), 2.72(2H,q,J = 7.6Hz), 3.89(2H,s), 4.50(1H,dt,J = 7.2, 7.3 Hz), 5.45(2H,s), 6.57(1H,s), 7.34(1H,d,J = 7.6Hz), 7.53(1H,s), 7.78(1H,d,J = 7.9Hz), 8.02(1H,dd,J = 7.6, 7.9Hz), 8.03(1H,dd,J = 7.6, 7.6Hz), 8.23(1H,d,J = 7.6Hz), 8.45(1H,d,J = 8.2Hz),	
94	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.43(3H,d,J = 7.3Hz), 2.59 (3H,s), 2.71(2H,q,J = 7.6Hz), 3.72(3H,s), 3.74(2H,s), 4.61(1H, qd,J = 7.1Hz), 5.39(2H,s), 6.49(1H,s), 7.06(1H,d,J = 7.3Hz), 7.51 (1H,s), 7.72(1H,d,J = 7.3Hz), 7.76(1H,dd,J = 7.9, 7.6Hz), 8.00(1H, dd,J = 7.9, 7.6Hz), 8.27(1H,d,J = 8.6Hz), 8.34(1H,d,J = 8.3Hz)	
95	(solvent:$CDCl_3$/MeoD(4/1)) 1.28(3H,t,J = 7.6Hz), 2.60(3H,s), 2.72(2H,q,J = 7.6Hz), 3.77(2H,s), 3.97(2H,s), 3.99(2H,s), 5.38 (2H,s), 6.53(1H,s), 7.14(1H,d,J = 7.6Hz), 7.37(1H,s), 7.75(1H,d, J = 7.9Hz), 7.79(1H,dd,J = 7.6, 8.2Hz), 8.02(1H,dd,J = 7.6, 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.30(1H,d,J = 8.2Hz)	

Table 90

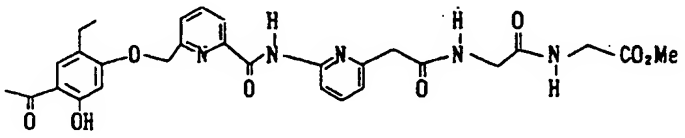
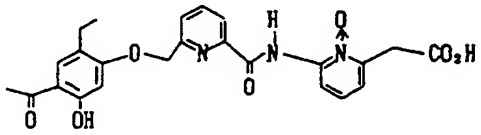
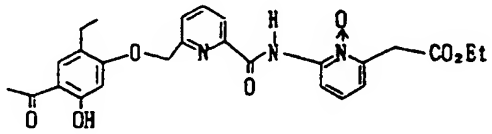
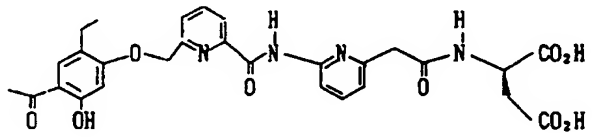
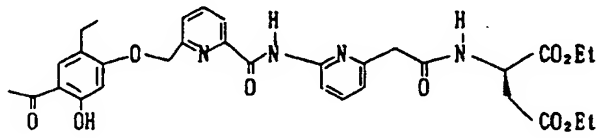
Ex. No.	Structural formula
96	
97	
98	
99	
100	

Table 91

	^{1}H-NMR	δppm
96	(solvent:$CDCl_3$) 1.21(3H,t,J = 7.1Hz), 1.27(3H,t,J = 7.4Hz), 2.58 (3H,s), 2.71(2H,q,J = 7.4Hz), 3.78(2H,s), 4.0-4.1(4H,m), 4.12 (2H,q,J = 7.1Hz), 5.40(2H,s), 6.52(1H,s), 7.07(1H,d,J = 7.3Hz), 7.50((1H,s), 7.72(1H,d,J = 7.9Hz), 7.76(1H,t,J = 8.3, 7.6Hz), 7.99 (1H,dd,J = 7.9, 7.9Hz), 8.27(1H,d,J = 8.6Hz), 8.30(1H,d,J = 8.9Hz)	
97	(solvent:DMSO-d_6) 1.30(3H,t,J = 7.6Hz), 2.59(3H,s), 2.72(2H,q,J = 7.6Hz), 3.49(1H,s), 4.13(2H,s), 5.40(2H,s), 6.48(1H,s), 7.17 (1H,dd,J = 1.8Hz,7.9Hz), 7.51(1H,s), 7.61(1H,dd,J = 7.9Hz,8.3Hz), 7.76(1H,d,J = 7.9Hz), 8.02(1H,dd,J = 7.9Hz, 7.9Hz), 8.26(1H,d,J = 8.6 Hz), 8.75(1H,dd,J = 1.8Hz,8.3Hz), 12.18(1H,br), 12.63(1H,s),	
98	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.31(1H,t,J = 7.1Hz), 2.58 (3H,s), 2.70(2H,q,J = 7.6Hz), 3.99(2H,s), 4.26(2H,q,J = 7.1Hz), 5.35(2H,s), 6.46(1H,s), 7.11(1H,dd,J = 1.7Hz,7.9Hz), 7.36(1H,dd, J = 7.9Hz,7.9Hz), 7.49(1H,s), 7.72(1H,dd,J = 1.0Hz,7.9Hz), 7.98 (1H,dd,J = 7.9Hz,7.9Hz), 8.23(1H,dd,J = 1.0Hz,7.9Hz), 8.63(1H,dd, J = 2.0Hz,8.6Hz), 12.29(1H,br), 12.62(1H,s)	
99	(solvent:$CDCl_3$) 1.29(3H,t,J = 7.4Hz), 2.57(3H,s), 2.72(2H,t,J = 7.4Hz), 2.96(1H,dd,J = 17.0, 4.5Hz), 3.09(1H,dd,J = 17.0, 4.5Hz), 3.77(2H,s), 4.85(1H,br), 5.49(2H,d,J = 3.3Hz), 6.72(1H,s), 7.02 (1H,d,J = 8.3Hz), 7.49(1H,s), 7.65(1H,d,J = 7.9Hz), 7.75(1H,dd,J = 7.6, 8.3Hz), 7.94(1H,dd,J = 7.6, 8.3Hz), 7.94(1H,dd,J = 7.9, 7.6 Hz), 8.19(1H,d,J = 7.6Hz), 8.32(1H,d,J = 8.3Hz)	
100	(solvent:$CDCl_3$) 1.10(3H,t,J = 7.0Hz), 1.17(3H,t,J = 7.1Hz), 1.28 (3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.85(1H,dd,J = 17.0, 4.6Hz), 3.02(1H,dd,J = 17.0, 4.6Hz), 3.75(2H,s), 4.00(2H, q,J = 7.1Hz), 4.16(2H,q,J = 7.0Hz), 4.85(1H,qt,J = 7.6, 4.6Hz), 5.39 (2H,s), 6.49(1H,s), 7.05(1H,d,J = 7.3Hs), 7.51(1H,s), 7.72(1H,d, J = 7.6Hz), 7.73(1H,dd,J = 7.3, 7.6Hz), 7.99(1H,dd,J = 7.6, 7.9Hz), 8.27(1H,d,J = 7.3Hz), 8.34(1H,d,J = 8.3Hz)	

EP 0 516 069 A1

Table 92

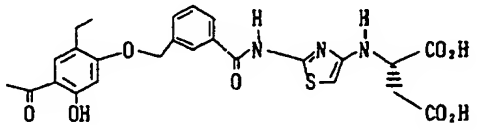
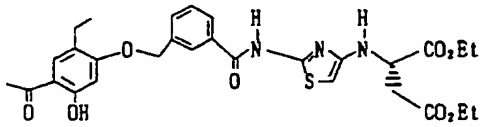
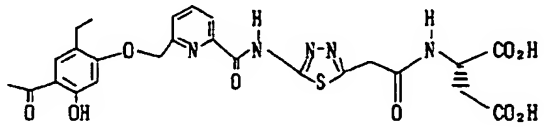
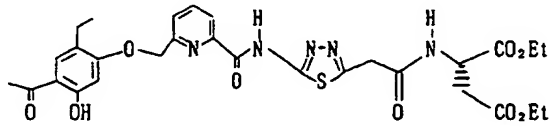
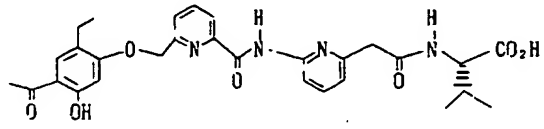
Ex. No.	Structural formula
101	
102	
103	
104	
105	

Table 93

	^{1}H-NMR δppm
101	(solvent:DMSO-d_6) 1.17(3H,t,J = 7.6Hz), 2.56(3H,s), 2.59(1H,m), 2.69(1H,m), 3.59(2H,s), 3.6-4.3(2H,br), 4.56(1H,m), 5.29(2H, s), 6.60(1H,s), 6.96(1H,s), 7.56(1H,t,J = 7.9Hz), 7.64(1H,s), 7. 68(1H,d,J = 7.9Hz), 8.07(1H,d,J = 7.9Hz), 8.19(1H,s), 8.23(1H,d,J = 7.6Hz), 12.6(1H,s)
102	(solvent:$CDCl_3$/DMSO-d_6(10/1)) 1.15-1.31(9H,m), 2.57(3H,s), 2.64(2H,q,J = 7.3Hz), 2.84(1H,dd,J = 17.2, 4.6Hz), 3.03(1H,dd,J = 17.2, 4.3Hz), 3.67(2H,s), 4.15-4.27(4H,m), 4.85(1H,ddd,J = 7.9, 4.6, 4.3Hz), 5.19(1H,s), 6.46(1H,s), 6.78(1H,s), 7.48(1H,s), 7.57(1H,t,J = 7.9Hz), 7.69(1H,d,J = 7.9Hz), 7.94(1H,brd,J = 8.3Hz), 7.97(1H,d,J = 7.9Hz), 8.10(1H,s), 12.68(1H,s)
103	(solvent:DMSO0-d_6) 1.21(3H,t,J = 7.3Hz), 2.58(H,s), 2.6-2.7(4H, m), 4.08(1H,s), 4.60(1H,m), 5.46(2H,s), 5.6-6.4(2H,br), 6.62 (1H,s), 7.68(1H,s), 7.80(2H,d), 8.15(2H,m), 8.78(1H,d,J = 7.9 Hz), 12.55(1H,s)
104	(solvent:$CDCl_3$) 1.23-1.65(9H,m), 2.59(3H,s), 2.70(2H,q,J = 7.3 Hz), 2.85(1H,dd,J = 17.2, 4.6Hz), 3.05(1H,dd,J = 17.2, 4.6Hz), 4.10(2H,s), 4.15(2H,q,J = 7.3Hz), 4.22(2H,q,J = 7.3Hz), 4.87(1H, dt,J = 7.9, 4.6Hz), 5.32(1H,s), 6.45(1H,s), 7.24(,1H,brd), 7.52 (1H,s), 7.75(1H,d,J = 7.3Hz), 8.01(1H,t,J = 7.9Hz), 8.26(1H,d,J = 7.9Hz), 12.67 (1H,s)
105	(solvent:DMSO-d_6) 0.96(6H,m), 1.30(3H,t,J = 7.6Hz), 2.17(1H,m), 2.58(3H,s), 2.73(2H,q,J = 7.6Hz), 3.75(2H,m), 4.67(1H,m), 5.42 (2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.9Hz), 7.51(1H,s), 7.65(1H,d, J = 7.9Hz), 7.75(1H,t,J = 7.9Hz), 7.95(1H,t,J = 7.9Hz), 8.22(1H,d,J = 7.9Hz), 8.32(1H,d,J = 7.9Hz), 8.91(1H,brd), 10.87(1H,s)

Table 94

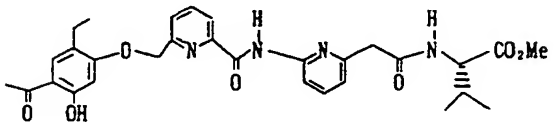
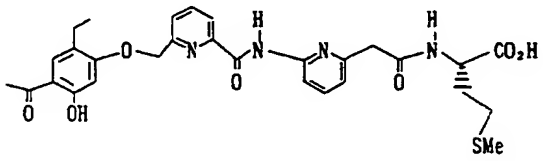
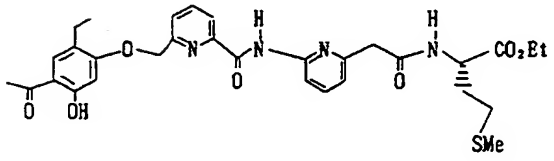
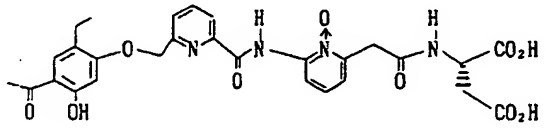
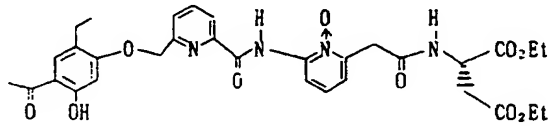
Ex. No.	Structural formula
106	
107	
108	
109	
110	

Table 95

	^{1}H-NMR δppm
106	(solvent:$CDCl_3$) 0.91(3H,m), 1.27(3H,t,J = 7.3Hz), 2.18(1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.3Hz), 3.71(3H,s), 3.76(2H,s), 4.60 (1H,s), 5.34(2H,s), 6.46(1H,s), 7.05(1H,d,J = 7.6Hz), 7.51(1H, s), 7.73(1H,t,J = 7.6Hz), 7.78(1H,d,J = 7.9Hz), 7.97(1H,br), 8.00 (1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.35(1H,d,J = 7.9Hz), 10.54 (1H,s), 12.62(1H,s)
107	(solvent:DMSO-d_6) 1.31(3H,t,J = 7.6Hz), 2.01(3H,s), 2.15(1H,m), 2.35(1H,m), 2.55(2H,m), 2.58(3H,s), 2.74(2H,q,J = 7.6Hz), 3.80 (1H,d,J = 15.8Hz), 3.68(1H,d,J = 15.8Hz), 4.73(1H,m), 5.48(2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.6Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6 Hz), 7.75(1H,t,J = 7.6Hz), 7.94(1H,t,J = 7.6Hz), 8.22(1H,d,J = 7.6 Hz), 8.33(1H,d,J = 7.6Hz), 9.08(1H,brd), 10.87(1H,s)
108	(solvent-$CDCl_3$) 1.1-1.3(6H,m), 2.00(3H,s), 2.05-2.2(2H,m), 2.47(2H,m), 2.59(3H,s), 2.70(2H,q,J = 7.3Hz), 3.74(2H,s), 4.16 (2H,m), 4.71(1H,m), 5.40(2H,s), 6.50(1H,s), 7.06(1H,d,J = 7.6 Hz), 7.51(1H,s), 7.75(1H,t,J = 7.6Hz), 7.77(1H,d,J = 7.9Hz), 7.96 (1H,br), 8.00(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.3Hz), 8.34(1H,d,J = 8.3Hz), 10.53(1H,s), 12.63(1H,s)
109	(solvent:DMSO-d_6) 1.21(3H,t,J = 7.3Hz), 2.51(3H,s), 2.63(4H,m), 3.89(2H,s), 4.59(1H,m), 5.42(2H,s), 6.63(1H,s), 7.29(1H,d,J = 8.3Hz), 7.44(1H,t,J = 8.3Hz), 7.65(1H,s), 7.83(1H,d,J = 7.3Hz), 8.18(1H,t,J = 7.3Hz), 8.23(1H,brd), 8.47(1H,d,J = 8.3Hz), 8.59(1H, d,J = 7.3Hz), 12.16(1H,s), 12.51(1H,s), 12.6(2H,br)
110	(solvent:$CDCl_3$) 1.15(3H,t,J = 7.3Hz), 1.17(3H,t,J = 7.3Hz), 1.27 (3H,t,J = 7.3Hz), 2.59(3H,s), 2.71(1H,q,J = 7.3Hz), 2.83(1H,dd,J = 16.8Hz,5.3Hz), 2.94(1H,dd,J = 16.8Hz,5.3Hz), 3.96(1H,d,J = 13.5 Hz), 4.07(1H,d,J = 13.5Hz), 4.11(2H,q,J = 7.3Hz), 4.12(2H,q,J = 7.3H z),4.81(1H,dt,J = 8.2Hz,5.3Hz), 5.39(2H,s), 6.48(1H,s), 7.18(1H, dd,J = 7.9Hz,1.7Hz), 7.41(1H,t,J = 7.9Hz), 7.50(1H,s), 7.76(1H,d, J = 7.9Hz), 8.01(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.63(1H,dd, J = 7.4Hz,1.7Hz), 8.69(1H,d,J = 8.2Hz), 12.32(1H,s), 12.61(1H,s)

Table 96

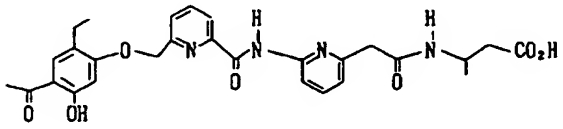
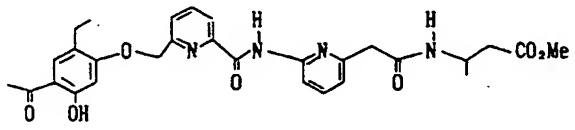
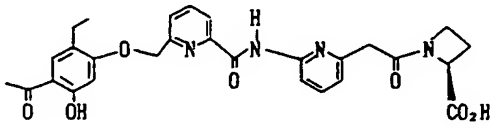
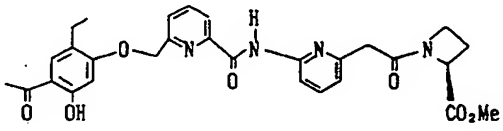
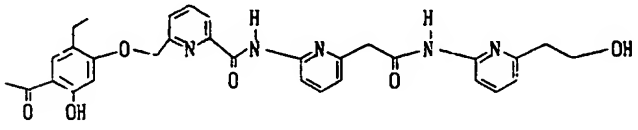
Ex. No.	Structural formula
111	
112	
113	
114	
115	

Table 97

	^{1}H-NMR	δppm
111	(solvent:DMSO-d_6) 1.12(3H,d,J = 6.6Hz), 1.22(3H,t,J = 7.6Hz), 2.30 (1H,dd,J = 15.2Hz,7.3Hz), 2.46(1H,dd,J = 15.2Hz,7.3Hz), 2.58(3H, s), 2.67(2H,q,J = 7.6Hz), 3.56(2H,s), 4.10(1H,m), 5.47(2H,s), 6.64(2H,s), 7.13(1H,d,J = 7.6Hz), 7.69(1H,s), 7.80-7.86(2H,m), 8.10-8.30(4H,m), 10.35(1H,s), 12.17(1H,s), 12.56(1H,s)	
112	(solvent:$CDCl_3$) 1.26(6H,m), 2.53(2H,d,J = 5.3Hz), 2.59(3H,s), 2.71(3H,s), 2.71(2H,m), 3.55(3H,s), 3.68(2H,s), 4.36(1H,m), 5.36(2H,s), 6.47(1H,s), 7.06(1H,d,J = 7.6Hz), 7.42(1H,brd,J = 7.9 Hz), 7.51(1H,s), 7.70(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.99 (1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.31(1H,d,J = 7.6Hz), 10.48 (1H,s), 12.65(1H,s)	
113	(solvent:DMSO-d_6) 1.23(3H,t,J = 7.3Hz), 2.14(1H,m), 2.6(1H,m), 2.58(3H,s), 2.67(2H,q,J = 7.3Hz), 3.45-3.70(2H,m), 3.83(1H,m), 4.22(1H,m), 5.02(0.4H,m), 4.57(0.6H,m), 5.48(2H,s), 6.65(1H, s), 7.14(1H,m), 7.69(1H,s), 7.65-7.90(2H,m), 8.15-8.30(3H,m), 10.32(0.6H,s), 10.34(0.4H,s), 12.55(1H,s), 12.90(1H,br)	
114	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.20-2.40(1H,m), 2.5-2.7 (1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.64(0.4H,s), 3.68(0.6 H,s), 3.77(0.6H,s), 3.80(0.4H,s), 4.05-4.40(2H,m), 4.79(0.6H, m), 4.95(0.4H,m), 5.34(2H,s), 6.48(1H,s), 7.13(0.4H,d,J = 7.6 Hz), 7.19(0.6H,d,J = 7.6Hz), 7.51(1H,s), 7.70(1H,d,J = 7.6Hz), 7.75(1H,m), 7.98(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.32(1H,d, J = 7.6Hz), 10.34(1H,s), 12.67(1H,s)	
115	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.6Hz), 2.58(3H,s), 2.72(2H,q,J = 7.6Hz), 2.91(2H,t,J = 5.7Hz), 3.87(2H,s), 3.92(2H,t,J = 5.7Hz), 5.46(2H,s), 6.60(1H,s), 6.88(1H,d,J = 7.3Hz), 7.12(1H,d,J = 6.6 Hz), 7.50(1H,s), 7.62(1H,dd,J = 7.6, 8.3Hz), 7.73(1H,d,J = 7.9Hz), 7.78(1H,dd,J = 7.6, 8.3Hz),7.98(1H,dd,J = 7.6 7.9Hz), 8.06(1H,d, J = 8.3Hz), 8.27(1H,d,J = 7.9Hz), 8.40(1H,d,J = 7.6Hz)	

Table 98

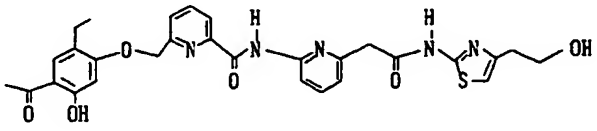
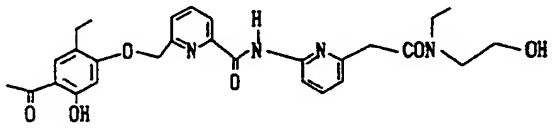
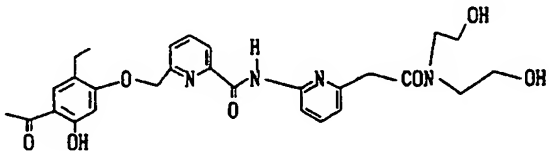
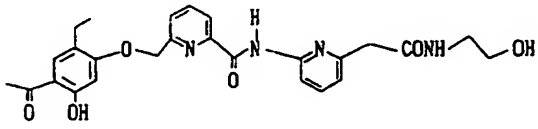
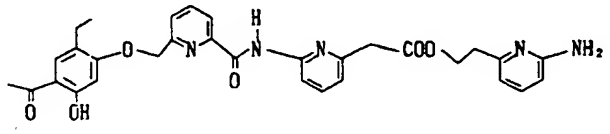
Ex. No.	Structural formula
116	
117	
118	
119	
120	

Table 99

	^{1}H-NMR	δppm
116	(solvent:$CDCl_3$/MeODC(1/4))1.28(3H,t,J = 7.6Hz), 2.60(3H,s), 2.72(2H,q,J = 7.6Hz), 2.88(2H,t,J = 6.3Hz), 3.86(2H,t,J = 6.3Hz), 3.97(2H,s), 5.39(2H,s), 6.52(1H,s), 6.68(1H,s), 7.19(1H,d,J = 7.6Hz), 7.55(1H,s), 7.76(1H,d,J = 7.9Hz), 7.83(1H,dd,J = 8.2,7.6Hz), 8.05(1H,dd,J = 7.6,J = 7.9Hz), 8.25(1H,d,J = 7.6Hz), 8.33(1H,d,J = 8.2Hz)	
117	(solvent:$CDCl_3$) 1.0-1.3(5H,m), 2.59(2H,s), 2.71(2H,q,J = 7.5Hz), 3.4-3.9(6H,m), 3.4-3.9(6H,m), 3.93(2H,s), 5.35(2H,s), 6.49(1H,s), 7.0-7.2(1H,m), 7.51(1H,s), 7.6-8.4(5H,m)	
118	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.58(3H,s), 2.70(2H,q,J = 7.4Hz), 3.6-4.0(8H,m), 4.00(2H,s), 5.35(2H,s), 6.51(1H,s), 7.11(1H,d,J = 7.6Hz), 7.50(1H,s), 7.70(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 7.6,7.6Hz), 7.97(1H,dd,J = 7.6,7.9Hz), 8.24(1H,d,J = 7.9Hz), 8.32(1H,d,J = 7.6Hz)	
119	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 2.60(3H,s), 2.71(2H,q,J = 7.4Hz), 3.42(2H,t,J = 6.6Hz), 3.68(2H,t,J = 6.6Hz), 3.71(2H,s), 5.37(2H,s), 6.50(1H,s), 7.13(1H,d,J = 7.6Hz), 7.53(1H,s), 7.74(1H,d,J = 7.6Hz), 7.76(1H,dd,J = 8.2,7.6Hz), 8.02(1H,dd,J = 7.6,7.6Hz), 8.25(1H,d,J = 7.6Hz), 8.27(1H,d,J = 8.2Hz)	
120	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.93(2H,t,J = 6.8Hz), 4.48(2H,t,J = 6.8Hz), 5.32(2H,s), 6.31(1H,d,J = 8.1Hz), 6.45(1H,d,J = 8.1Hz), 7.03(1H,d,J = 7.6Hz), 7.29(1H,d,J = 8.1,8.1Hz), 7.69(1H,d,J = 7.6Hz) 7.71(1H,dd,J = 7.6,7.6Hz), 7.97(1H,dd,J = 7.6,7.6Hz), 8.26(1H,d,J = 7.6Hz), 8.33(1H,d,J = 7.6Hz)	

Table 100

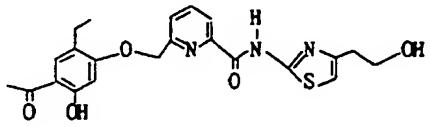
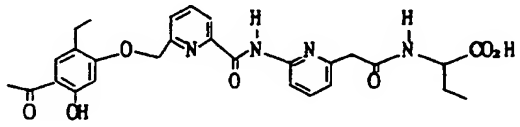
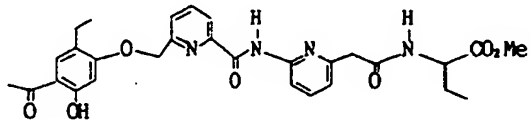
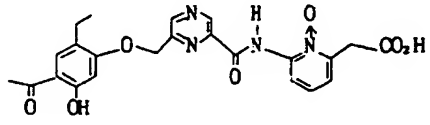
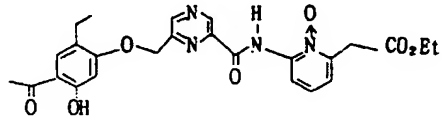
Ex. No.	Structural formula
121	
122	
123	
124	
125	

Table 101

	^{1}H-NMR δppm
121	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 2.59(3H,s), 2.71(2H,q,J = 7.4Hz), 2.96(2H,t,J = 5.5Hz), 3.96(2H,t,J = 5.5Hz), 5.33(2H,s), 6.45(1H,s), 6.73(1H,s), 7.51(1H,s), 7.72(1H,d,J = 6.9Hz), 8.00(1H,dd,J = 7.9,7.6Hz), 8.25(1H,dd,J = 7.6Hz)
122	(solvent:DMSO-d_6) 0.41(3H,t,J = 7.6Hz), 1.30(3H,t,J = 7.6Hz), 1.7-1.9(2H,m), 2.57(3H,s), 3.74(2H,ABq,J = 15.4Hz,5.5Hz), 4.66(1H,m), 5.46(2H,s), 6.83(1H,s), 7.02(1H,d,J = 7.6Hz), 7.51(1H,s), 7.63(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.94(1H,t,J = 7.6Hz), 8.22(1H,d,J = 7.6Hz), 8.32(1H,d,J = 7.6Hz), 8.94(1H,m), 10.86(1H,s)
123	(solvent:$CDCl_3$) 0.88(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 1.7-1.9(2H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.71(3H,s), 3.74(2H,s), 4.63(1H,m), 5.37(2H,s), 6.47(1H,s), 7.06(1H,d,J = 7.6Hz), 7.71(1H,d,J = 7.6Hz), 7.75(1H,t,J = 7.6Hz), 7.86(1H,m), 8.00(1H,t,J = 7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.35(1H,m,J = 7.6Hz), 10.53(1H,s), 12.63(1H,s)
124	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.59(3H,s), 2.65(2H,q,J = 7.6Hz), 3.89(2H,s), 5.53(2H,s), 6.73(1H,s), 7.37(1H,d,J = 7.9Hz), 7.51(1H,t,J = 7.9Hz), 7.69(1H,s), 8.46(1H,d,J = 7.9Hz), 9.13(1H,s), 9.37(1H,s), 11.96(1H,s), 12.50(1H,br), 12.54(1H,s)
125	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.31(3H,t,J = 7.3Hz), 2.60(3H,s), 2.69(2H,q,J = 7.6Hz), 3.98(3H,s), 4.25(2H,q,J = 7.3Hz), 5.39(2H,s), 6.47(1H,s), 7.15(1H,dd,J = 8.3Hz, 2.0Hz), 7.39(1H,t,J = 8.3Hz), 7.52(1H,s), 8.61(1H,dd,J = 8.3Hz,2.0Hz), 9.07(1H,s), 9.46(1H,s), 12.12(1H,s) , 12.65(1H,s)

Table 102

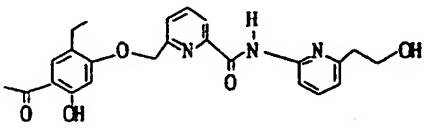
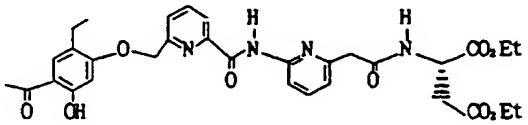
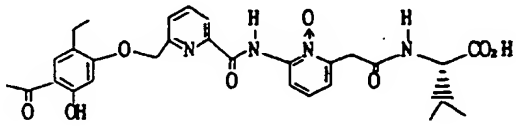
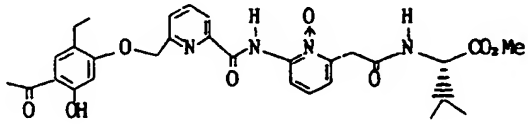
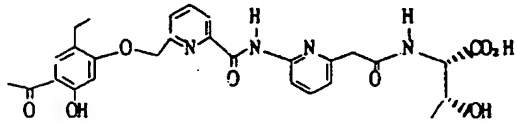
Ex. No.	Structural formula
126	
127	
128	
129	
130	

Table 103

	^{1}H-NMR δppm
126	(solvent:$CDCl_3$) 1.28(3H,t,J = 7.4Hz), 2.58(3H,s), 2.71(2H,q,J = 7.4Hz), 3.02(2H,t,J = 5.5Hz), 4.05(2H,t,J = 5.5Hz), 5.34(2H,s), 6.49(1H,s), 6.98(1H,d,J = 7.6Hz), 7.50(1H,s), 7.70(1H,d,J = 7.9Hz), 7.72(1H,dd,J = 7.9,7.9Hz), 7.98(1H,d,J = 7.9,7.6Hz), 8.27(1H,d,J = 7.6Hz), 8.30(1H,d,J = 8.2Hz)
127	(solvent:$CDCl_3$) 1.10(3H,t,J = 7.1Hz), 1.17(3H,t,J = 7.3Hz), 1.27(3H,t,J = 8.1Hz), 2.59(3H,s), 2.71(2H,q,J = 7.2Hz), 2.84(1H,dd,J = 16.8,4.6Hz), 3.02(1H,dd,J = 16.8,4.3Hz), 3.75(2H,s), 4.00(2H,q,J = 7.1Hz), 4.16(2H,q,J = 7.0Hz), 4.85(1H,dt,J = 7.9,4.6Hz), 5.39(2H,s), 6.49(1H,s), 7.05(1H,dd,J = 7.6,0.6Hz), 7.51(1H,s), 7.72(1H,d,J = 7.6Hz), 7.75(1H,dd,J = 7.9,7.9Hz), 7.99(1H,dd,J = 7.6,7.9Hz), 8.26(1H,dd,J = 8.6,1.0Hz), 8.34(1H,dd,J = 8.2,0.7Hz)
128	(solvent:DMSO-d_6) 0.90(3H,d,J = 7.6Hz), 0.91(3H,d,J = 7.6Hz), 1.19(3H,t,J = 7.3Hz), 2.07(1H,m), 2.58(3H,s), 2.65(2H,q,J = 7.3Hz) 3.92(2H,ABq,J = 21.8,15.5Hz), 4.18(1H,dd,J = 8.3,5.6Hz), 5.42(2H,s), 6.62(1H,s), 7.29(1H,dd,J = 8.3,2.0Hz), 7.48(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(1H,m), 8.20(2H,m), 8.45(1H,dd,J = 8.3,2.0Hz), 8.46(1H,d,J = 8.3Hz), 12.17(1H,s), 12.51(1H,s), 12.60(1H,s)
129	(solvent:$CDCl_3$) 0.88(3H,t,J = 7.3Hz), 0.89(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 2.18(1H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz) 3.65(3H,s), 4.04(2H,ABq,J = 17.5,13.2Hz), 4.40(1H,m), 5.36(2H,s) 6.45(1H,s), 7.18(1H,dd,J = 8.3,2.0Hz), 7.41(1H,t,J = 8.3Hz), 7.51(1H,s), 7.74(1H,d,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.63(1H,dd,J = 8.3,2.0Hz), 8.7δ(1H,d,J = 8.6Hz), 12.38(1H,s), 12.62(1H,s)
130	(solvent:DMSO-d_6) 1.10(3H,d,J = 7.3Hz), 1.22(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.76(2H,ABq,J = 20.5,14.9Hz), 4.17(1H,br), 4.26(1H,m), 4.95(1H,m), 5.47(2H,s), 6.63(1H,s), 7.20(1H,d,J = 7.6Hz), 7.69(1H,s), 7.82(2H,m), 8.18(4H,m), 10.36(1H,s), 12.50(1H,br), 12.55(1H,s)

Table 104

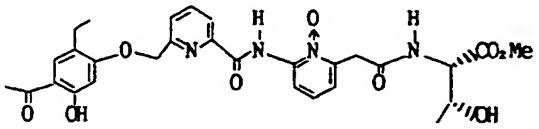
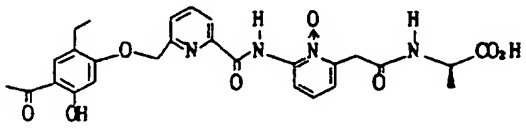
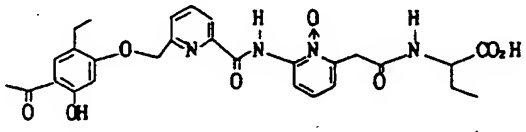
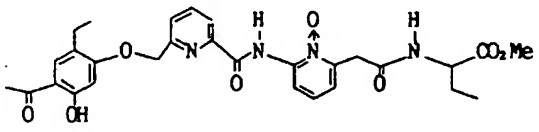
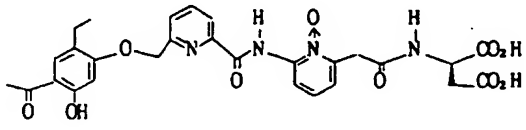
Ex. No.	Structural formula
131	
132	
133	
134	
135	

Table 105

	^{1}H-NMR δppm
131	(solvent:$CDCl_3$) 1.16(3H,d,J = 7.3Hz), 1.26(3H,t,J = 7.6Hz), 2.57(3H,s), 2.69(2H,q,J = 7.6Hz), 3.01(1H,br), 3.69(3H,s), 4.05(2H,ABq,J = 20.1Hz,13.9Hz), 4.50(1H,m), 4.54(1H,m), 5.36(2H,s), 6.49(1H,s), 7.20(1H,dd,J = 8.3Hz, 1.7Hz), 7.41(1H,t,J = 8.3Hz), 7.48(1H,s), 7.72(1H,d,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.21(1H,d,J = 7.9Hz), 8.51(1H,d,J = 8.6Hz), 8.60(1H,dd,J = 8.3,1.7Hz), 12.34(1H,s), 12.64(1H,s)
132	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.3Hz), 1.31(3H,d,J = 7.3Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.85(2H,m), 4.24(1H,m), 5.43(2H,s), 6.63(1H,s), 7.31(1H,dd,J = 8.3,1.7Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.85(1H,m), 8.21(2H,m), 8.46(1H,dd,J = 8.3,1.7Hz), 8.54(1H,d,J = 7.9Hz), 12.15(1H,s), 12.50(1H,s), 12.55(1H,br)
133	(solvent:DMSO-d_6) 0.92(3H,t,J = 7.6Hz), 1.20(3H,t,J = 7.6Hz), 1.6-1.9(1H,m), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 3.89(2H,ABq,J = 20.8,15.8Hz), 4.17(1H,m), 5.42(2H,s), 6.63(1H,s), 7.30(1H,dd,J = 8.3Hz,2.0Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s) 7.85(2H,m), 8.21(2H,m), 8.45(1H,dd,J = 8.3,2.0Hz), 8.50(1H,d,J = 7.9Hz), 12.16(1H,s), 12.50(1H,s), 12.55(1H,br)
134	(solvent:$CDCl_3$) 0.89(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.6Hz), 1.70-1.85(2H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.66(3H,s), 4.02(2H,ABq,J = 18.8,13.2Hz), 4.45(1H,m), 5.38(2H,s), 6.48(1H,s), 7.18(1H,dd,J = 7.9,2.0Hz), 7.41(1H,t,J = 7.9Hz), 7.50(1H,s), 7.75(1H,d,J = 7.9Hz), 8.00(1H,t,J = 7.9Hz), 8.25(1H,d,J = 7.9Hz), 8.61(1H,brd), 8.63(1H,dd,J = 7.9Hz,2.0Hz), 12.33(1H,s), 12.63(1H,s)
135	(solvent:DMSO-d_6) 1.20(3H,t,J = 7.6Hz), 2.58(3H,s), 2.65(2H,q,J = 7.6Hz), 2.7-2.9(2H,m), 3.87(2H,s), 4.58(1H,m), 5.43(2H,s), 6.64(1H,s), 7.30(1H,dd,J = 8.3,2.0Hz), 7.47(1H,t,J = 8.3Hz), 7.68(1H,s), 7.84(1H,m), 8.21(1H,m), 8.46(1H,dd,J = 8.3Hz,2.0Hz), 8.61(1H,d,J = 7.9Hz), 12.14(1H,s), 12.51(1H,s), 12.55(2H,br)

Table 106

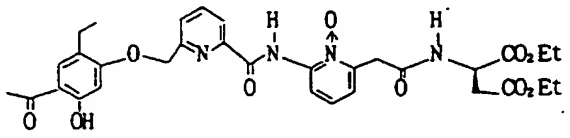
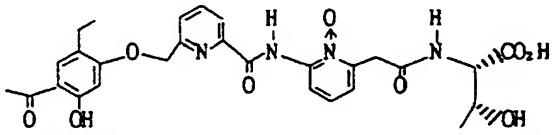
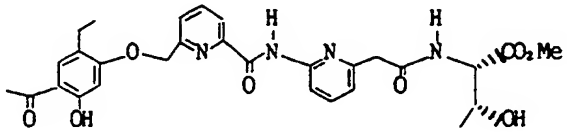
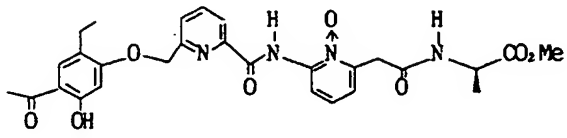
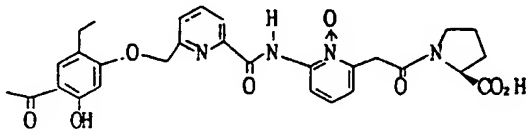
Ex. No.	Structural formula
136	
137	
138	
139	
140	

Table 107

	^{1}H-NMR δppm
136	(solvent:$CDCl_3$) 1.15(3H,t,J=7.3Hz), 1.17(3H,t,J=7.3Hz), 1.27(3H,t,J=7.6Hz), 2.59(3H,s), 2.71(2H,q,J=7.6Hz), 2.80-2.95(2H,m), 3.93-4.16(6H,m), 4.81(1H,m), 5.39(2H,s), 6.47(1H,s), 7.18(1H,d,J=8.3Hz), 7.41(1H,t,J=8.3Hz), 7.51(1H,s), 7.76(1H,d,J=7.9Hz), 8.01(1H,t,J=7.9Hz), 8.25(1H,d,J=7.9Hz), 8.62(1H,dd,J=8.3,1.7Hz), 8.69(1H,d,J=7.9Hz), 12.31(1H,s), 12.61(1H,s)
137	(solvent:DMSO-d_6) 1.09(3H,d,J=7.6Hz), 1.20(3H,t,J=7.6Hz), 2.58(3H,s), 2.66(2H,q,J=7.6Hz), 3.96(2H,ABq,J=20.8,15.8Hz), 4.10(1H,br), 4.24(1H,m), 4.90(1H,m), 5.42(2H,s), 6.63(1H,s), 7.31(1H,dd,J=7.9,2.0Hz), 7.48(1H,t,J=7.9Hz), 7.68(1H,s), 7.85(1H,m), 8.17-8.30(3H,m), 12.16(1H,s), 12.50(1H,s), 12.55(1H,br)
138	(solvent:$CDCl_3$) 1.18(2H,d,J=6.6Hz), 1.27(3H,t,J=7.6Hz), 2.58(3H,s), 2.69(2H,q,J=7.6Hz), 3.72(3H,s), 3.80(2H,s), 4.34(4H,m), 4.61(1H,m), 5.37(2H,s), 6.49(1H,s), 7.06(1H,d,J=7.9Hz), 7.49(1H,s), 7.70(1H,d,J=7.9Hz), 7.76(1H,t,J=7.9Hz), 7.97(1H,t,J=7.9Hz), 8.25(1H,d,J=7.9Hz), 8.29(1H,d,J=7.9Hz), 8.46(1H,brd,J=8.3Hz), 10.57(1H,s), 12.70(1H,s)
139	(solvent:$CDCl_3$) 1.27(3H,t,J=7.6Hz), 1.41(3H,d,J=7.3Hz), 2.59(3H,s), 2.71(2H,q,J=7.6Hz), 3.66(3H,s), 4.01(2H,ABq,J=29.7Hz,13.2Hz), 4.51(1H,m), 5.40(2H,s), 6.50(1H,s), 7.18(1H,dd,J=8.3,2.0Hz), 7.41(1H,t,J=8.3Hz), 7.50(1H,s), 7.75(1H,d,J=7.9Hz), 8.00(1H,t,J=7.9Hz), 8.26(1H,d,J=7.9Hz), 8.52(1H,d,J=7.6Hz), 8.64(1H,dd,J=8.3,2.0Hz), 12.31(1H,s), 12.63(1H,s)
140	(solvent:DMSO-d_6) 1.20(3H,t,J=7.6Hz), 1.90-2.52(4H,m), 2.58(3H,s), 2.66(2H,q,J=7.6Hz), 3.70(2H,m), 3.99(2H,ABq,J=29.7,16.2Hz), 4.29(1H,m), 5.24(2H,s), 6.63(1H,s), 7.33(1H,dd,J=7.6,2.0Hz), 7.47(1H,t,J=8.3Hz), 7.68(1H,s), 7.85(1H,dd,J=5.6,3.3Hz), 8.20(2H,s), 8.46(1H,dd,J=8.3,2.0Hz), 12.14(1H,s), 12.51(1H,s)

Table 108

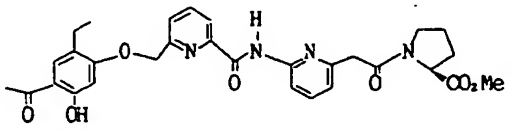
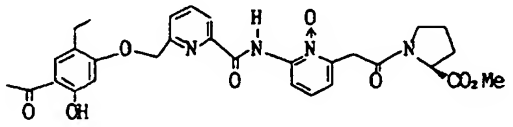
Ex. No.	Structural formula
141	
142	

Table 109

	^{1}H-NMR	δppm
141	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.59(3H,s), 2.71(2H,q,J = 7.6Hz), 3.73(3H,s), 3.6-3.9(2H,m), 3.87(2H,m), 4.55(1H,m), 5.33(2H,s), 6.47(1H,s), 7.18(1H,d,J = 7.9Hz), 7.51(1H,s), 7.69(1H,d,J = 7.9Hz), 7.74(1H,t,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.27(1H,d,J = 7.9Hz), 8.31(1H,d,J = 7.9Hz), 10.34(1H,s), 12.67(1H,s)	
142	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.70(2H,q,J = 7.6Hz), 3.74(3H,s), 3.7-3.9(2H,m), 3.90(1H,d,J = 15.8Hz), 4.26(1H,d,J = 15.8Hz), 4.61(1H,m), 5.35(2H,s), 6.46(1H,s), 7.25(1H,brd), 7.37(1H,t,J = 7.9Hz), 7.50(1H,s), 7.73(1H,d,J = 7.9Hz), 7.98(1H,t,J = 7.9Hz), 8.24(1H,d,J = 7.9Hz), 8.59(1H,d,J = 7.9Hz), 12.29(1H,s), 12.65(1H,s)	

Table 110

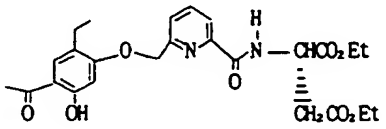
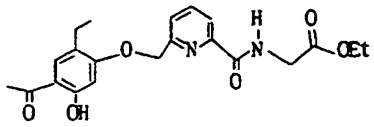
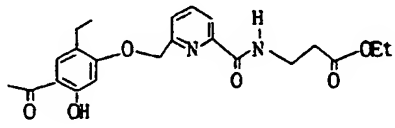
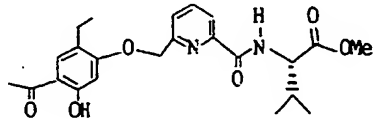
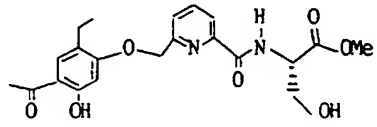
Ex. No.	Structural formula
143	
144	
145	
146	
147	

Table 111

	^{1}H-NMR	δppm
143	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.4Hz), 1.27(3H,t,J = 7.4Hz), 1.30(3H,t,J = 7.0Hz), 2.58(3H,t), 2.69(2H,q,J = 7.4Hz), 2.97(1H,dd,J = 16.8,4.6Hz), 3.13(1H,dd,J = 16.8,4.0Hz), 4.19(2H,qd,J = 7.3,3.0Hz), 4.27(2H,q,J = 7.3, 3.0Hz) 5.06(1H,td,J = 8.3,5.0Hz), 5.27(1H,s), 6.46(1H,s), 7.49(1H,s), 7.64(1H,dd,J = 7.6,1.0Hz), 7.91(1H,dd,J = 7.6,7.6Hz), 8.14(1H,dd,J = 7.6,1.0Hz)	
144	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 4.2-4.3(4H,m), 5.26(2H,s), 6.45(1H,s), 7.49(1H,s), 7.64(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 6.9,7.6Hz), 8.15(1H,d,J = 6.9Hz), 12.66(1H,s)	
145	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 1.28(3H,t,J = 7.3Hz), 2.6-2.7(4H,m), 3.7-3.8(2H,m), 4.1-4.2(2H,q,J = 7.3Hz), 5.24(2H,s), 6.45(1H,s), 7.49(1H,s), 7.61(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 6.6,7.9Hz), 8.14(1H,d,J = 6.6Hz), 8.42(1H,br), 12.66(1H,s)	
146	(solvent:$CDCl_3$) 1.02(6H,dd,J = 4.0Hz,6.9Hz), 1.26(3H,t,J = 7.6Hz) , 2.2-2.4(1H,m), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.78(3H,s), 4.75(1H,dd,J = 5.3,9.2Hz), 5.29(2H,s), 6.49(1H,s), 7.50(1H,s), 7.64(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.9,7.9Hz), 8.15(1H,d,J = 7.9Hz), 8.44(1H,d,J = 9.2Hz), 12.66(1H,s)	
147	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.85(3H,s), 4.0-4.2(2H,m), 4.8-4.9(1H,m), 5.29(2H,s), 6.51(1H,s), 7.49(1H,s), 7.65(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 7.6,7.9Hz), 8.15(1H,d,J = 7.9Hz), 8.80(1H,d,J = 7.9Hz), 12.70(1H,s)	

Table 112

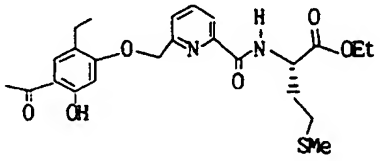
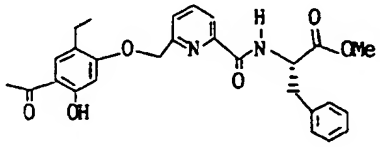
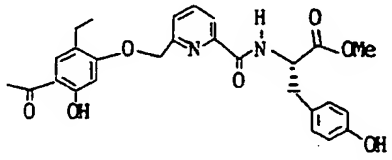
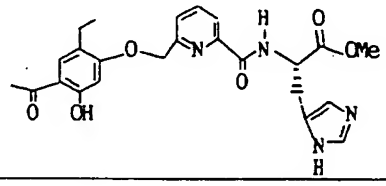
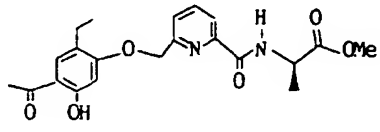
Ex. No.	Structural formula
148	
149	
150	
151	
152	

Table 113

	^{1}H-NMR	δppm
148	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.3Hz), 2.0-2.2(1H,m), 2.12(3H,s), 2.3-2.4(1H,m), 2.5-2.7(4H,m), 2.58(3H,s), 4.26(2H,q,J = 7.3Hz), 4.8-5.0(1H,m), 5.29(2H,s), 6.47(1H,s), 7.50(1H,s), 7.64(1H,dd,J = 1.0,7.6Hz), 7.91,(1H,dd,J = 7.6,7.6Hz), 8.14(1H,dd,J = 1.0Hz,7.6Hz), 8.52(1H,d,J = 8.6Hz), 12.66(1H,s)	
149	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.26(2H,dd,J = 1.8Hz,6.3Hz), 3.75(3H,s), 5.07(1H,dt,J = 8.3,6.3Hz), 5.22(2H,s), 6.45(1H,s), 7.1-7.4(5H,m), 7.50(1H,s), 7.62(1H,d,J = 7.3Hz), 7.89(1H,dd,J = 6.9Hz,7.3Hz), 8.11(1H,d,J = 6.9Hz), 8.41(1H,d,J = 8.3Hz), 12.67(1H,s)	
150	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.1-3.2(2H,m), 3.76(3H,s), 5.02(1H,dt,J = 8.6Hz,5.9Hz), 5.21(2H,d,J = 2.0Hz), 6.09(1H,s), 6.42(1H,s), 6.76(1H,dd,J = 2.3Hz,8.9Hz), 7.02(1H,d,J = 8.9Hz), 7.50(1H,s), 7.61(1H,d,J = 7.6Hz), 7.88(1H,dd,J = 7.5Hz,7.6Hz), 8.10(1H,d,J = 7.5Hz), 8.40(1H,d,J = 8.6Hz), 12.63(1H,s)	
151	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.30(2H,d,J = 5.6Hz), 3.79(3H,s), 5.0-5.1(1H,m), 5.27(2H,d,J = 4.62Hz), 6.42(1H,s), 6.86(1H,d,J = 1.3Hz), 7.49(1H,s), 7.6-7.7(2H,m), 7.89(1H,dd,J = 7.6Hz,7.6Hz), 8.12(1H,dd,J = 1.0Hz,7.9Hz), 8.8-8.9(1H,m), 12.80(1H,s)	
152	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.57(3H,d,J = 6.9Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.80(3H,s), 4.82(1H,dq,J = 6.9Hz,8.3Hz), 5.28(2H,s), 6.47(1H,s), 7.50(1H,s), 7.63(1H,dd,J = 1.0Hz,7.9Hz), 7.91(1H,dd,J = 7.9Hz,7.9Hz), 8.14(1H,dd,J = 1.0,7.9Hz), 8.43(1H,d,J = 8.3Hz), 12.66(1H,s)	

Table 114

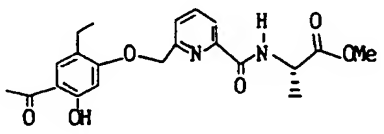
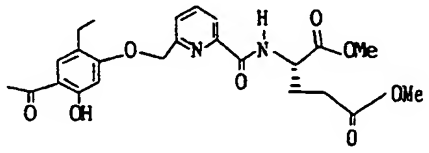
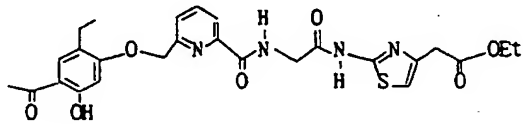
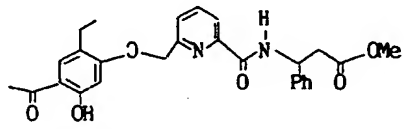
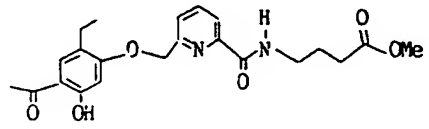
Ex. No.	Structural formula
153	
154	
155	
156	
157	

Table 115

	^{1}H-NMR	δppm
153	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 1.57(3H,d,J = 7.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.80(3H,s), 4.82(1H,dq,J = 7.3Hz,7.9Hz), 5.28(2H,s), 6.45(1H,s), 7.50(1H,s), 7.63(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6,7.6Hz), 8.14(1H,d,J = 7.6Hz), 8.43(1H,d,J = 7.9Hz), 12.66(1H,s)	
154	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.6Hz), 2.1-2.5(4H,m), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.66(3H,s), 3.70(3H,s), 4.8-4.9(1H,m), 5.29(2H,s), 6.48(1H,s), 7.50(1H,s), 7.64(1H,dd,J = 1.0Hz,7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.13(1H,dd,J = 1.0,7.6Hz), 8.47(1H,d J = 8.6Hz), 12.65(1H,s)	
155	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.3Hz), 1.26(3H,t,J = 7.6Hz), 2.58(3H,s), 2.69(2H,q,J = 7.6Hz), 3.68(2H,d,J = 1.0Hz), 4.17(2H,q,J = 7.3Hz), 4.42(2H,d,J = 6.3Hz), 5.26(2H,s), 6.45(1H,s), 6.82(1H,t,J = 1.0Hz), 7.50(1H,s), 7.69(1H,d,J = 7.9Hz), 7.96(1H,dd,J = 7.9Hz,8.9Hz), 8.63(1H,br), 9.80(1H,br), 12.67(1H,s)	
156	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 2.97(1H,dd,J = 6.3Hz,15.8Hz), 3.09(1H,dd,J = 6.6,15.8Hz), 3.64(3H,s), 5.27(2H,s), 5.64(1H,ddd,J = 6.3Hz,6.6Hz,8.9Hz), 6.49(1H,s), 7.2-7.5(5H,m), 7.49(1H,s), 7.63(1H,d,J = 7.3Hz), 7.90(1H,dd,J = 7.3Hz,7.3Hz), 8.15(1H,d,J = 7.3Hz), 8.80(1H,d,J = 8.9Hz), 12.66(1H,s)	
157	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 1.9-2.1(2H,m), 2.45(2H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.54(2H,m), 3.68(3H,s), 5.25(2H,s), 6.47(1H,s), 7.50(1H,s), 7.61(1H,d,J = 7.6Hz), 7.90(1H,dd,J = 7.6Hz,7.9Hz), 8.10(1H,br), 8.15(1H,d,J = 7.9Hz)	

Table 116

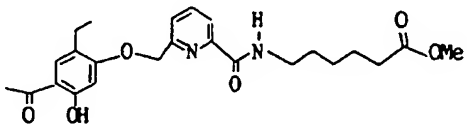
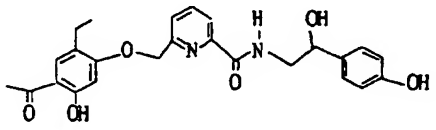
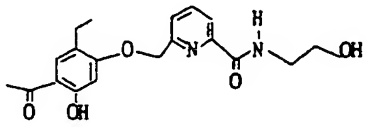
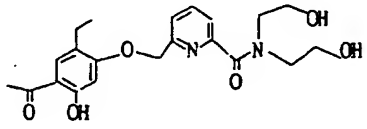
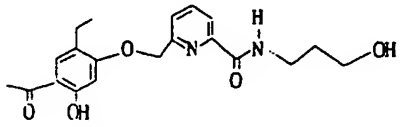
Ex. No.	Structural formula
158	
159	
160	
161	
162	

Table 117

	^{1}H-NMR	δppm
158	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 1.3-1.5(2H,m), 1.6-1.8(4H,m), 2.34(2H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.4-3.5(2H,m), 3.67(3H,s), 5.25(2H,s), 6.47(1H,s), 7.49(1H,s), 7.51(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 7.9Hz,7.9Hz), 8.02(1H,br), 8.16(1H,d,J = 7.9Hz), 12.67(1H,s)	
159	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.52(3H,s), 2.60(2H,q,J = 7.6Hz), 3.5-3.7(2H,m), 4.6-4.8(1H,m), 5.36(2H,s), 5.57(1H,d,J = 4.3Hz), 6.58(1H,s), 6.6-6.7(1H,m), 6.8-6.9(2H,m), 7.1-7.2(1H,m), 7.7-7.8(2H,m), 7.9-8.2(2H,m), 8.5-8.6(1H,m), 9.34(1H,s), 12.56(1H,s)	
160	(solvent:DMSO-d_6) 1.25(3H,t,J = 7.6Hz), 2.59(3H,s), 2.67(2H,q,J = 7.6Hz), 2.73(1H,t,J = 5.4Hz), 3.6-3.7(2H,m), 3.8-3.9(2H,m), 5.25(2H,m), 6.49(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.16(1H,d,J = 7.6Hz), 8.40(1H,br), 12.69(1H,s)	
161	(solvent:DMSO-d_6) 1.24(3H,t,J = 7.6Hz), 2.59(3H,s), 2.68(2H,q,J = 7.6Hz), 3.6-4.0(9H,m), 5.25(2H,s), 5.84(1H,t,J = 4.6Hz), 6.43(1H,s), 7.49(1H,s), 7.62(1H,d,J = 7.6Hz), 7.81(1H,d,J = 7.6Hz), 7.95(1H,dd,J = 7.6Hz,7.6Hz), 12.62(1H,s)	
162	(solvent:DMSO-d_6) 1.25(3H,t,J = 7.6Hz), 1.8-1.9(2H,m), 2.58(3H,s), 2.67(2H,q,J = 7.6Hz), 3.30(1H,t,J = 6.4Hz), 5.25(2H,s), 6.50(1H,s), 7.63(1H,d,J = 7.6Hz), 7.91(1H,dd,J = 7.6Hz,7.6Hz), 8.16(1H,d,J = 7.6Hz), 8.30(1H,br), 12.71(1H,s)	

Table 118

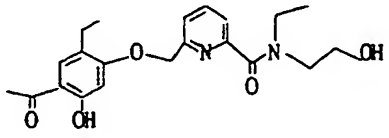
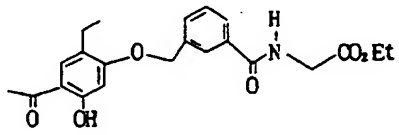
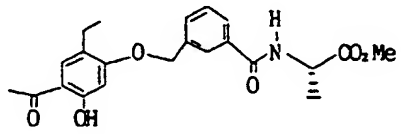
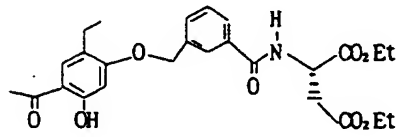
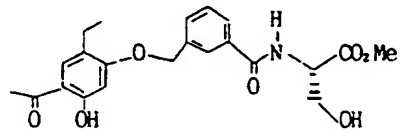
Ex. No.	Structural formula
163	
164	
165	
166	
167	

Table 119

	^{1}H-NMR	δppm
163	(solvent:DMSO-d_6) 1.25(3H,t,J = 7.6Hz), 1.32(3H,t,J = 7.1Hz), 2.57(3H,s), 2.68(2H,q,J = 7.6Hz), 3.4-4.0(6H,m), 5.25(2H,s), 6.45(1H,s), 7.49(1H,s), 7.5-7.9(3H,m), 12.61(1H,s)	
164	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.4Hz), 1.32(3H,t,J = 7.1Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 4.26(2H,s), 4.27(2H,q,J = 7.1Hz), 5.13(2H,s), 6.44(1H,s), 7.46(1H,s), 7.49(1H,dd,J = 7.6,7.6Hz), 7.59(1H,d,J = 7.6Hz), 7.77(1H,d,J = 7.6Hz), 7.90(1H,s)	
165	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.4Hz), 1.54(2H,d,J = 7.0Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 3.80(3H,s), 4.82(1H,q,J = 7.0Hz), 5.14(2H,s), 6.44(1H,s), 7.46(1H,s), 7.48(1H,dd,J = 7.6,7.6Hz), 7.58(1H,q,J = 7.6Hz), 7.76(1H,d,J = 7.6Hz), 7.88(1H,s)	
166	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.6Hz), 1.26(3H,t,J = 7.1Hz), 1.29(3H,t,J = 7.1Hz), 2.57(3H,s), 2.64(2H,q,J = 7.4Hz), 2.97(1H,dd,J = 17.2,4.3Hz), 3.14(1H,dd,J = 17.2,4.3Hz), 4.16(2H,q,J = 7.1Hz), 4.27(2H,q,J = 7.1Hz), 5.04(1H,td,J = 4.3,7.9Hz), 5.15(1H,s), 6.45(1H,s), 7.46(1H,s), 7.49(1H,dd,J = 7.6,7.6Hz), 7.59(1H,d J = 7.6Hz), 7.77(1H,d,J = 7.6Hz), 7.90(1H,s)	
167	(solvent:$CDCl_3$) 1.22(3H,t,J = 7.4Hz), 2.57(3H,s), 2.63(2H,q,J = 7.4Hz), 3.83(3H,s), 4.1-4.2(2H,br), 4.89(1H,dt,J = 7.3,3.6Hz), 5.14(2H,s), 6.44(1H,s), 7.47(1H,s), 7.49(1H dd,J = 7.6,7.6Hz), 7.60(1H,d,J = 7.6Hz), 7.80(1H,d,J = 7.6Hz), 7.91(1H,s)	

Table 120

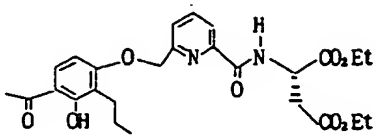
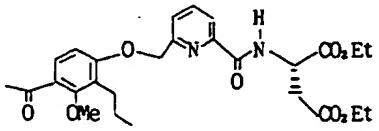
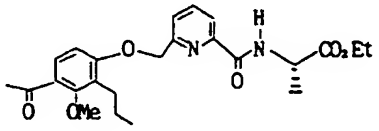
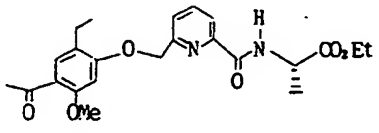
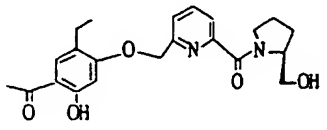
Ex. No.	Structural formula
168	
169	
170	
171	
172	

Table 121

	^{1}H-NMR	δppm
168	(solvent:$CDCl_3$) 0.98(3H,t,J = 7.3Hz), 1.27(3H,t,J = 7.3Hz), 1.30(3H,t,J = 7.1Hz), 1.5-1.7(2H,m), 2.58(3H,s), 2.76(2H,t,J = 7.6Hz), 2.98(1H,dd,J = 16.8,4.9Hz), 3.14(1H,dd,J = 16.8,4.9Hz), 4.1-4.4(4H,m), 5.06(1H,dt,J = 8.6,4.9Hz), 5.32(2H,s), 6.50(1H,d,J = 8.9Hz), 7.61(1H,d,J = 8.9Hz), 7.66(1H,d,J = 8.9Hz), 7.66(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.13(1H,d,J = 7.6Hz)	
169	(solvent:$CDCl_3$) 1.02(3H,t,J = 7.4Hz), 1.27(3H,t,J = 7.1Hz), 1.30(3H,t,J = 7.1Hz), 1.6-1.7(2H,m), 2.62(3H,t), 2.74(2H,t,J = 7.9Hz), 2.97(1H,dd,J = 17.0,4.9Hz), 3.13(1H,dd,J = 17.0,4.9Hz), 4.1-4.4(4H,m), 5.06(1H,dt,J = 8.3,4.9Hz), 5.29(2H,s), 6.74(1H,d,J = 8.8Hz), 7.57(1H,d,J = 8.8Hz), 7.66(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
170	(solvent:$CDCl_3$) 1.02(3H,t,J = 7.3Hz), 1.32(3H,t,J = 7.3Hz), 1.56(3H,d,J = 7.3Hz), 1.6-1.7(2H,m), 2.62(3H,s), 2.75(2H,t,J = 7.9Hz), 3.78(3H,s), 4.26(2H,q,J = 7.2Hz), 4.79(1H,qd,J = 7.8,7.8Hz), 5.29(2H,s), 6.73(1H,d,J = 7.6Hz), 7.57(1H,d,J = 8.6Hz), 7.64(1H,d,J = 7.9Hz), 7.91(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
171	(solvent:$CDCl_3$) 1.24(3H,t,J = 7.2Hz), 11.32(3H,t,J = 7.1Hz), 1.56(3H,d,J = 1.0Hz), 2.58(3H,s), 2.69(2H,q,J = 7.5Hz), 3.88(3H,s), 4.26(2H,q,J = 7.2Hz), 4.81(1H,qd,J = 7.7,7.7Hz), 5.32(2H,s), 6.51(1H,s), 7.72(1H,s), 7.70(1H,d,J = 8.3Hz), 7.93(1H,dd,J = 9.7,7.6Hz), 8.15(1H,d,J = 7.9Hz)	
172	(solvent:$CDCl_3$) 1.24(3H,t,J = 7.5Hz), 1.6-2.2(4H,m), 2.57(3H,s), 2.67(2H,q,J = 7.5Hz), 3.5-5.4(7H,m), 6.44-6.46(2H,m), 7.5-8.0(4H,m),	

Table 122

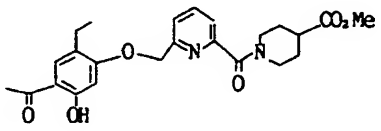
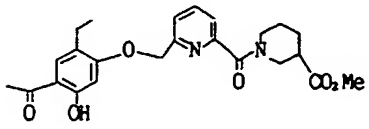
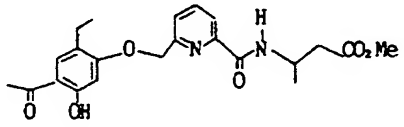
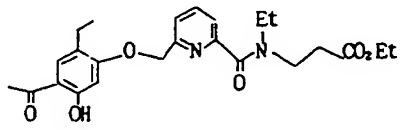
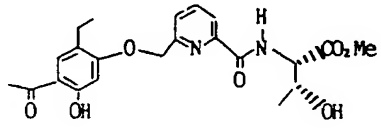
Ex. No.	Structural formula
173	
174	
175	
176	
177	

Table 123

	^{1}H-NMR	δppm
173	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.5Hz), 1.7-2.1(5H,m), 2.57(3H,s), 2.67(2H,q,J = 7.5Hz), 3.0-3.3(2H,m), 3.72(3H,s), 3.8-4.0(2H,m), 4.5-4.7(2H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.53(1H,d,J = 7.6Hz), 7.56(1H,d,J = 7.6Hz), 7.84(1H,dd,J = 7.9,7.9Hz)	
174	(solvent:$CDCl_3$) 1.25(3H,td,J = 7.6,2.0Hz), 1.5-2.0(4H,m), 2.57(3H,s), 2.68(2H,q,J = 7.6Hz), 3.61(1.5H,s), 3.73(1.5H,s), 2.5-5.0(5H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.5-8.0(3H,m)	
175	(solvent:$CDCl_3$) 1.26(3H,t,J = 7.4Hz), 1.38(2H,d,J = 6.9Hz), 2.58(3H,s), 2.5-2.7(4H,m), 3.72(3H,s), 4.5-4.6(1H,m), 5.27(2H,s), 6.48(1H,s), 7.49(1H,s), 7.61(1H,d,J = 7.9Hz), 7.89(1H,dd,J = 7.9,7.6Hz), 8.15(1H,d,J = 7.6Hz)	
176	(solvent:$CDCl_3$) 1.22(3H,t,J = 6.9Hz), 1.25(3H,t,J = 7.1Hz), 1.29(3H,t,J = 7.1Hz), 2.57(3H,s), 2.68(2H,q,J = 7.4Hz), 2.78(1H,t,J = 7.1Hz), 3.44(1H,q,J = 7.1Hz), 3.58(1H,q,J = 7.1Hz), 3.70(1H,t,J = 7.4Hz), 3.79(1H,t,J = 7.4Hz), 4.10(1H,q,J = 7.1Hz), 4.18(1H,q,J = 7.1Hz), 5.21(1H,s), 5.23(1H,s), 6.43(1H,s), 7.48(1H,s), 7.5-7.9(3H,m), 2.84(1H,t,J = 7.1Hz)	
177	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.4Hz), 1.29(3H,d,J = 6.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 4.4-4.6(1H,m), 4.7-4.9(1H,m), 5.30(2H,s), 6.50(1H,s), 7.50(1H,s), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.13(1H,d,J = 7.6Hz)	

Table 124

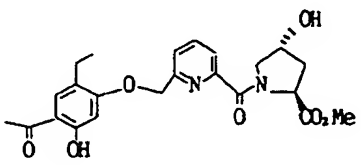
Ex. No.	Structural formula
178	

Table 125

	^{1}H-NMR	δppm
178	(solvent:$CDCl_3$) 1.23(1.2H,t,J = 7.6Hz), 1.26(1.8H,t,J = 7.6Hz), 2.1-2.6(2H,m), 2.59(3H,s), 2.8-3.0(2H,m), 3.8-4.8(3H,m), 5.3-5.4(3H,m), 6.44(0.6H,s), 6.48(0.4H,s), 7.5-8.1(3H,s)	

Table 126

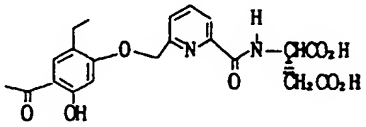
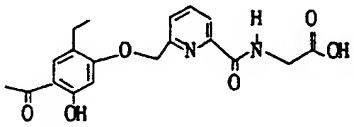
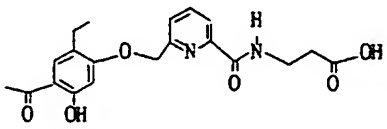
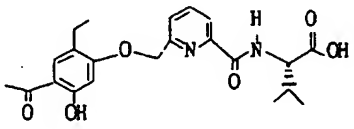
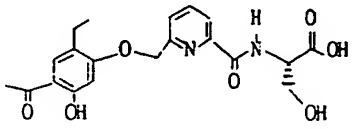
	^{1}H-NMR δ ppm
179	
180	
181	
182	
183	

Table 127

	^{1}H-NMR	δppm
179	(solvent: $CD_3OD/CDCl_3$(1/4)) 1.26(3H,t,J=7.4Hz), 2.60(3H,s), 2.70(2H,q,J=7.4Hz), 2.97(1H,dd,J=17.5,4.8Hz), 3.15(1H,dd,J=17.5,4.8Hz), 5.00(1H,t,J=8.9Hz), 5.29(2H,s), 6.47(1H,s), 7.53(1H,s), 7.68(1H,d,J=7.9Hz), 7.95(1H,dd,J=7.9,7.6Hz), 8.11(1H,d,J=7.6Hz)	
180	(solvent:d_6-DMSO) 1.18(3H,t,J=7.6Hz), 2.58(3H,S), 2.62(2H,q,J=7.6Hz), 4.00(2H,d,J=5.9Hz), 5.36(2H,s), 6.57(1H,s), 7.69(1H,s), 7.73(1H,d,J=6.3Hz), 8.01(1H,d,J=6.3Hz), 8.10(1H,dd,J=6.3Hz,6.3Hz), 8.88(1H,t,J=5.9Hz), 12.55(1H,s)	
181	(solvent:d_6-DMSO) 1.18(3H,s,J=7.6Hz), 2.58(3H,s), 2.61(2H,q,J=7.6Hz), 2.69(2H,q,J=7.6Hz), 3.4-3.5(2H,m), 5.35(2H,s), 6.57(1H,s) 7.69(1H,s), 7.70(1H,dd,J=1.0Hz,7.6Hz), 7.99(1H,dd,J=1.0Hz,7.6Hz), 8.07(1H,dd,J=7.6Hz,7.6Hz), 8.72(1H,t,J=5.9Hz), 12.54(1H,br)	
182	(solvent:d_6-DMSO) 0.91(6H,t,J=6.4Hz), 1.18(3H,t,J=7.6Hz), 2.1-2.2(1H,m), 2.57(3H,s), 2.63(1H,q,J=7.6Hz), 4.41(1H,dd,J=5.1Hz,8.9Hz), 5.42(2H,s), 6.63(1H,s), 7.68(1H,s), 7.76(1H,d,J=6.6Hz), 8.01(1H,d,J=6.9Hz), 8.11(1H,dd,J=6.6Hz,6.9Hz), 8.38(1H,d,J=8.9Hz), 12.55(1H,s)	
183	(solvent:d_6-DMSO) 1.19(3H,t,J=7.6Hz), 2.58(3H,s), 2.63(2H,q,J=7.6Hz), 3.77(1H,dd,J=3.6Hz,10.9Hz), 3.91(1H,dd,J=3.6Hz,10.9Hz), 4.4-4.5(1H,s) 5.39(2H,s) 6.61(1H,s), 7.69(1H,s), 7.75(1H,d,J=7.6Hz), 8.03(1H,dd,J=1.0Hz,7.6Hz), 8.11(1H,dd,J=7.6Hz,7.6Hz), 8.63(1H,d,J=8.3Hz), 12.55(1H,s)	

Table 128

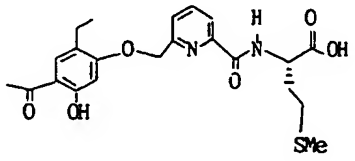
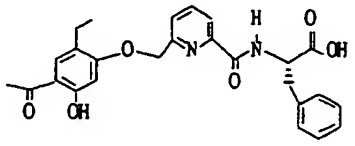
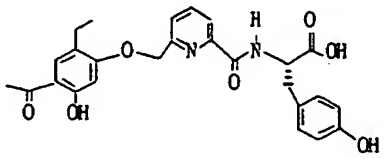
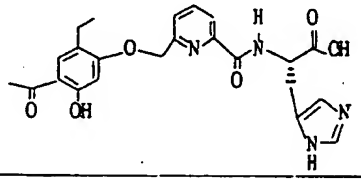
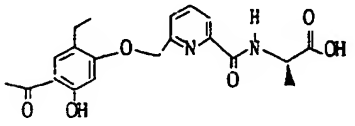
Ex. No.	Structural formula
184	
185	
186	
187	
188	

Table 129

	^{1}H-NMR δppm
184	(solvent:d_6-DMSO) 1.18(3H,t,J = 7.6Hz), 2.04(3H,s), 2.1-2.2(2H,m), 2.4-2.5(2H,m), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 4.5-4.6(1H,m), 5.40(2H,s), 6.60(1H,s), 7.69(1H,s), 7.74(1H,d,J = 7.6Hz), 7.99(1H,d,J = 6.6Hz), 8.09(1H,dd,J = 6.6Hz,7.6Hz), 8.74(1H,d,J = 8.2Hz), 12.55(1H,s)
185	(solvent:d_6-DMSO) 1.16(3H,t,J = 7.6Hz), 2.59(3H,s), 2.63(2H,q,J = 7.6Hz), 3.1-3.4(2H,m), 4.6-4.7(1H,m), 5.34(2H,s), 6.60(1H,s), 7.1-7.3(5H,m), 7.68(1H,s), 7.71(1H,d,J = 7.6Hz), 7.97(1H,dd,J = 1.0Hz,7.6Hz), 8.07(1H,dd,J = 7.6Hz,7.6Hz), 8.61(1H,d,J = 8.2Hz), 12.56(1H,s)
186	(solvent:d_6-DMSO) 1.17(3H,t,J = 7.6Hz), 2.58(3H,s), 2.61(2H,q,J = 7.6Hz), 3.5-3.6(2H,m), 4.6-4.7(1H,m), 5.36(1H,s), 6.62(2H,d,J = 8.5Hz),6.99(2H,d,J = 8.5Hz), 7.69(1H,s), 7.73(1H,dd,J = 1.0Hz,7.6Hz), 7.96(1H,dd,J = 1.0Hz),7.6Hz) 8.08(1H,dd,J = 7.6Hz,7.6Hz), 8.52(1H,d,J = 8.3Hz), 9.21(1H,br), 12.56(1H,s)
187	(solvent:d_6-DMSO) 1.17(3H,t,J = 7.6Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 3.20(2H,d,J = 6.3Hz), 4.7-4.8(1H,m), 5.37(2H,s), 6.60(1H,s), 7.12(1H,s), 7.69(1H,s), 7.72(1H,d,J = 7.6Hz),7.98(1H,dd,J = 0.7Hz,7.6Hz) 8.08(1H,dd,J = 7.6Hz,7.6Hz), 8.28(1H,s) 8.99(1H,d,J = 8.3Hz), 12.54(1H,br),
188	(solvent:d_6-DMSO) 1.89(3H,t,J = 7.6Hz), 1.43(3H,d,J = 7.3Hz), 2.58(3H,s), 2.63(2H,q,J = 7.6Hz), 4.4-4.5(1H,m), 5.39(2H,s), 6.59(1H,s), 7.69(1H,s), 7.73(1H,d,J = 7.6Hz), 8.00(1H,d,J = 7.6Hz), 8.09(1H,dd,J = 7.6Hz,7.6Hz), 8.67(1H,d,J = 7.9Hz), 12.55(1H,s)

Table 130

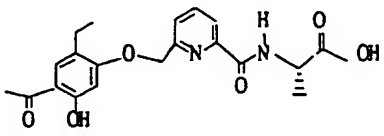
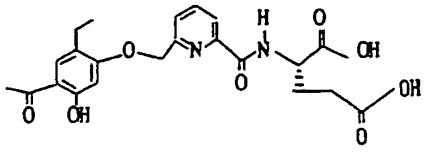
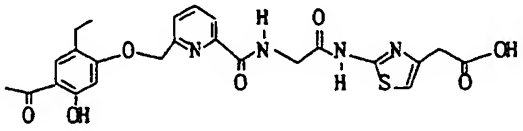
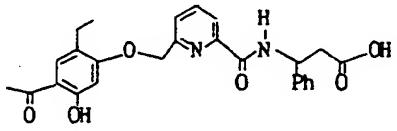
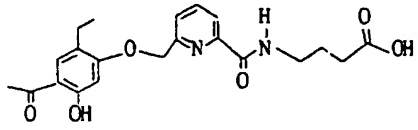
Ex. No.	Structural formula
189	
190	
191	
192	
193	

Table 131

	^{1}H-NMR	δppm
189	(solvent:d_6-DMSO) 1.89(3H,t,J=7.6Hz), 1.43(3H,d,J=7.3Hz), 2.58(3H,s), 2.63(2H,q,J=7.6Hz), 4.4-4.5(1H,m), 5.39(2H,s), 6.59(1H,s), 7.69(1H,s), 7.73(1H,d,J=7.6Hz), 8.00(1H,d,J=7.6Hz), 8.09(1H,dd,J=7.6Hz,7.6Hz), 8.67(1H,d,J=7.9Hz), 12.55(1H,s)	
190	(solvent:d_6-DMSO) 1.86(3H,t,J=7.6Hz), 1.9-2.3(4H,m), 2.58(3H,s), 2.63(2H,q,J=7.6Hz), 4.4-4.5(1H,m), 5.40(2H,s), 6.60(1H,s), 7.69(1H,s), 7.73(1H,d,J=7.6Hz), 8.00(1H,d,J=7.6Hz), 8.10(1H,dd,J=7.6Hz,7.6Hz), 8.70(1H,d,J=8.6Hz), 12.55(1H,s)	
191	(solvent:d_6-DMSO) 1.19(3H,t,J=7.6Hz), 2.58(3H,s), 2.63(2H,q,J=7.6Hz), 3.60(2H,s), 4.24(2H,d,J=5.9Hz), 5.38(2H,s), 6.58(1H,s), 6.96(1H,s), 7.70(1H,s), 7.75(1H,d,J=7.6Hz), 8.02(1H,d,J=7.6Hz), 8.10(1H,dd,J=7.6Hz,7.6Hz), 8.98(1H,d,J=5.9Hz), 12.34(1H,br), 12.55(1H,s)	
192	(solvent:d_6-DMSO) 1.17(3H,t,J=7.6Hz), 2.58(3H,s), 2.62(2H,q,J=7.6Hz), 2.88(1H,dd,J=6.3Hz,16.2Hz), 4.0-4.2(1H,m), 5.39(2H,s), 5.4-5.5(1H,m), 6.60(1H,s), 7.2-7.7(5H,m), 7.69(1H,s), 7.72(1H,d,J=7.6Hz), 7.98(1H,d,J=7.3Hz), 8.07(1H,dd,J=7.3Hz,7.6Hz), 9.13(1H,d,J=8.9Hz), 12.32(1H,br), 12.56(1H,s)	
193	(solvent:d_6-DMSO) 1.18(3H,t,J=7.6Hz), 1.7-1.8(2H,m), 2.26(2H,t,J=7.6Hz), 2.58(3H,s), 2.62(2H,q,J=7.6Hz), 3.3-3.5(2H,m), 5.36(2H,s), 6.57(1H,s), 7.69(1H,s), 7.70(1H,d,J=7.6Hz), 7.98(1H,d,J=7.6Hz), 8.06(1H,dd,J=7.6Hz,7.6Hz), 8.68(1H,d,J=5.6Hz), 12.00(1H,br), 12.55(1H,br)	

Table 132

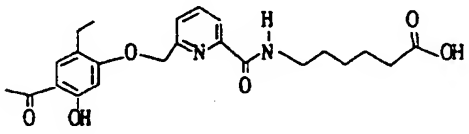
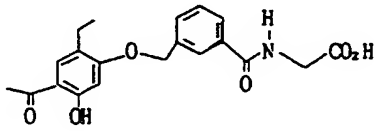
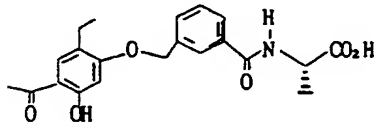
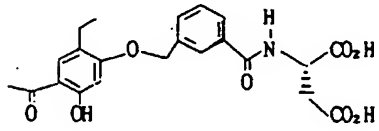
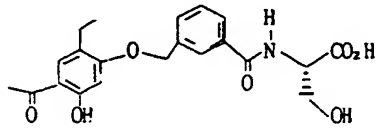
Ex. No.	Structural formula
194	
195	
196	
197	
198	

Table 133

	^{1}H-NMR	δppm
194	(solvent:DMSO-d_6) 1.18(3H,t,J = 7.6Hz), 1.2-1.3(2H,m), 1.5-1.7(4H,m), 2.21(2H,t,J = 7.3Hz), 2.58(3H,s), 2.62(2H,q,J = 7.6Hz), 5.36(2H,s), 6.57(1H,s), 7.68(1H,d,J = 7.6Hz), 7.69(1H,s), 7.98(1H,d,J = 7.6Hz), 8.06(1H,dd,J = 7.6Hz,7.6Hz), 8.61(1H,m), 12.55(1H,br)	
195	(solvent:CD_3OD/$CDCl_3$(1/4)) 1.21(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 4.18(2H,d,J = 1.7Hz), 5.16(2H,s), 6.46(1H,s), 7.49(1H,s), 7.50(1H,dd,J = 7.6,7.6Hz), 7.61(1H,d,J = 7.6Hz), 7.81(1H,d,J = 7.6Hz), 7.91(1H,s),	
196	(solvent:CD_3OD:$CDCl_3$ = 1:4) 1.22(3H,t,J = 7.4Hz), 1.55(3H,d,J = 6.9Hz), 2.58(3H,s), 2.64(2H,q,J = 7.4Hz), 4.72(1H,td,J = 5.9,7.3Hz), 5.17(2H,s), 6.46(1H,s), 7.50(1H,dd,J = 7.9,7.6Hz), 7.61(1H,d,J = 7.9Hz), 7.80(1H,d,J = 7.6Hz), 7.90(1H,s)	
197	(solvent:CD_3OD:$CDCl_3$ = 1:4) 1.22(3H,td,J = 7.6,0.9Hz), 2.65(2H,q,J = 7.6Hz), 2.98(1H,dd,J = 17.2,5.0Hz), 3.11(1H,dd,J = 17.5,5.0Hz), 4.99(1H,dt,J = 4.3,8.6Hz), 5.18(2H,s), 6.47(1H,s), 7.51(1H,dd,J = 7.6,8.3Hz), 7.63(1H,d,J = 8.3Hz), 7.81(1H,d,J = 7.6Hz), 7.92(1H,s), 2.59(3H,s), 7.51(1H,s)	
198	(solvent:CD_3OD:$CDCl_3$ = 1:4) 1.22(3H,t,J = 7.4Hz), 2.58(3H,s), 2.64(2H,q,J = 7.4Hz), 3.97(1H,dd,J = 11.6,3.5Hz), 4.10(1H,dd,J = 11.2,3.9Hz), 4.67(1H,t,J = 3.6Hz), 5.17(1H,s), 6.46(1H,s), 7.50(1H,s), 7.51(1H,dd,J = 7.6,7.6Hz), 7,62(1H,d,J = 7.6Hz), 7.85(1H,d,J = 7.6Hz)	

Table 134

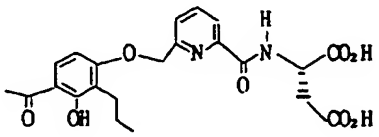
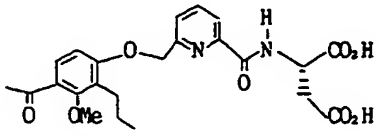
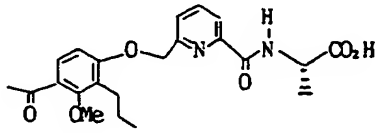
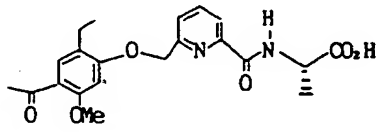
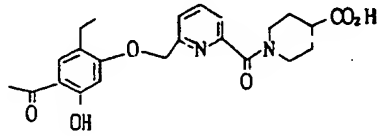
Ex. No.	Structural formula
199	
200	
201	
202	
203	

Table 135

	^{1}H-NMR	δppm
199	(solvent:$CD_3OD/CDCl_3$(1/4)) 0.99(3H,t,J = 7.6Hz), 1.5-1.7(2H,m), 2.60(3H,s), 2.70(2H,t,J = 7.8Hz), 3.0-3.3(2H,m), 5.1-5.2(1H,m), 5.27(2H,s) 6.76(2H,d,J = 8.9Hz), 7.53(2H,d,J = 8.9Hz), 7.64(1H,d,J = 7.9Hz), 7.90(1H,dd,J = 7.9,7.6Hz), 8.11(1H,d,J = 7.6Hz)	
200	(solvent:$CD_3OD/CDCl_3$(1/4)) 0.98(3H,t,J = 7.3Hz), 1.5-1.7(2H,m), 2.57(3H,s), 2.75(2H,t,J = 7.6Hz), 3.0-3.3(2H,m), 3.75(3H,s), 5.1-5.2(1H,m), 5.31(2H,s), 6.50(1H,d,J = 8.9Hz), 7.60(1H,d,J = 8.9Hz), 7.67(1H,d,J = 7.6Hz), 7.92(1H,dd,J = 7.6,7.3Hz), 8.14(1H,d,J = 7.3Hz)	
201	(solvent:$CD_3OD/CDCl_3$(1/4)) 1.01(3H,t,J = 7.3Hz), 1.63(3H,d,J = 7.3Hz), 1.5-1.7(2H,m), 2.62(3H,s), 2.74(2H,t,J = 7.6Hz), 3.78(3H,s), 4.80(1H,t,J = 7.3Hz), 5.29(2H,s), 6.73(1H,d,J = 8.9Hz), 7.55(1H,d,J = 8.9Hz), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.15(1H,d,J = 7.6Hz)	
202	(solvent:$CD_3OD/CDCl_3$(1/4)) 1.23(3H,t,J = 7.4Hz), 1.62(3H,d,J = 7.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 3.87(3H,s), 4.82(1H,q,J = 7.3,7.3Hz), 5.31(2H,s), 6.49(1H,s), 7.71(1H,d,J = 7.9Hz), 7.71(1H,s), 7.94(1H,dd,J = 7.6,7.9Hz), 8.16(1H,d,J = 7.6Hz)	
203	(solvent: $CD_3OD/CDCl_3$(1/4)) 1.24(3H,t,J = 7.6Hz), 1.7-2.2(4H,m), 2.57(3H,s), 2.6-2.8(1H,m), 2.67(2H,q,J = 7.6Hz), 3.0-3.3(2H,m), 3.8-4.0(1H,m), 4.4-4.6(1H,m), 5.25(2H,s), 6.44(1H,s), 7.47(1H,s), 7.54(1H,d,J = 7.6Hz), 7.57(1H,d,J = 7.0Hz), 7.85(1H,dd,J = 7.6,7.9Hz)	

Table 136

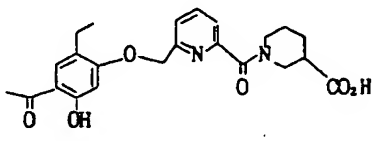
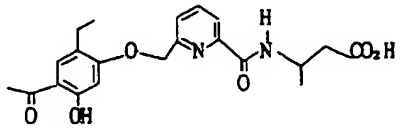
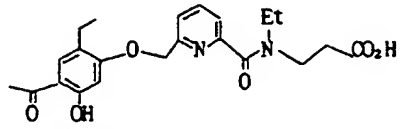
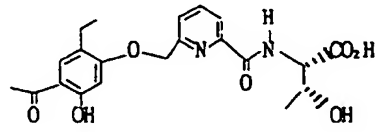
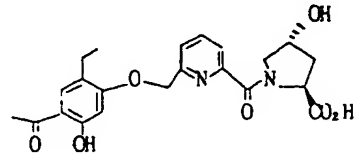
Ex. No.	Structural formula
204	
205	
206	
207	
208	

Table 137

	^{1}H-NMR	δppm
204	(solvent:$CD_3OD/CDCl_3$(1/4)) 1.25(3H,t,J = 7.4Hz), 1.5-2.3(5H,m), 2.57(3H,s), 2.67(2H,q,J = 7.4Hz), 2.7-2.9(1H,m), 3.1-4.8(4H,m), 5.25(2H,s), 6.44(1H,s), 7.47(1H,s), 7.5-7.7(2H,m), 7.85(1H,dd,J = 7.6,7.9Hz)	
205	(solvent: $CD_3OD/CDCl_3$(1/4)) 1.24(3H,t,J = 7.6Hz), 1.43(3H,d,J = 6.6Hz), 2.58(3H,s), 2.67(2H,q,J = 7.4Hz), 2.74(2H,dd,J = 5.6,3.0Hz), 4.5-4.6(1H,m), 5.25(2H,s), 6.51(1H,s), 7.48(1H,s), 7.61(1H,d,J = 7.9Hz), 7.89(1H,dd,J = 7.6,7.9Hz), 8.14(1H,d,J = 7.6Hz)	
206	(solvent:$CD_3OD/CDCl_3$(1/4)) 1.2-1.3(6H,m), 2.57(1H,s), 2.67(2H,q,J = 7.5Hz), 2.8-3.0(2H,m), 3.4-3.8(4H,m), 5.24(2H,s), 6.4-6.5(1H,m), 7.48(1H,s), 7.5-7.7(2H,m), 7.85(1H,dd,J = 7.6,7.9Hz),	
207	(solvent:$CD_3OD/CDCl_3$(1/9)) 1.25(3H,t,J = 7.4Hz), 1.29(3H,d,J = 6.3Hz), 2.58(3H,s), 2.69(2H,q,J = 7.4Hz), 4.4-4.6(1H,m), 4.7-4.9(1H,m), 5.30(2H,s), 6.50(1H,s), 7.50(1H,s), 7.66(1H,d,J = 7.6Hz), 7.93(1H,dd,J = 7.6,7.6Hz), 8.13(1H,d,J = 7.6Hz)	
208	(solvent: $CD_3OD/CDCl_3$(1/9)) 1.23(1.2H,t,J = 7.6Hz), 1.26(1.8H,t,J = 7.6Hz), 2.1-2.6(2H,m), 2.59(3H,s), 2.8-3.0(2H.m), 3.8-4.8(3H,m), 5.3-5.4(3H,m), 6.44(0.6H,s), 6.48(0.4H,s), 7.5-8.1(3H,s),	

Table 138

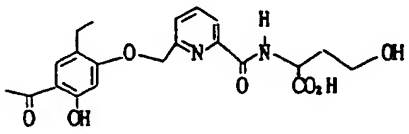
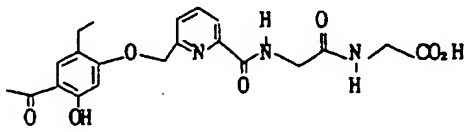
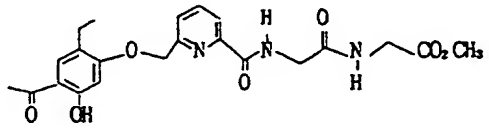
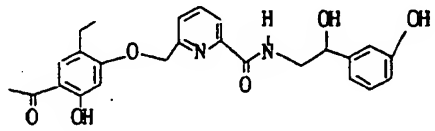
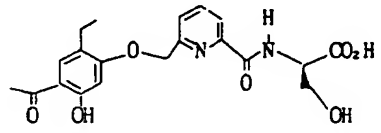
Ex. No.	Structural formula
209	
210	
211	
212	
213	

Table 139

	^{1}H-NMR	δppm
209	(solvent:$CDCl_3$/MeOD(9/1)) 1.26(3H,t,J = 7.4Hz), 1.9-2.1(1H,m), 2.2-2.4(1H,m), 2.59(3H,s), 2.70(1H,q,J = 7.4Hz), 3.6-3.9(1H,m), 4.84(1H,dt,J = 4,3,4.6Hz), 5.30(2H,s), 6.49(1H,s), 7.53(1H,s), 7.69(1H,d,J = 7.6Hz), 7.96(1H,dd,J = 7.6,7.6Hz), 8.11(1H,d,J = 7.6Hz)	
210	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.57(3H,s), 2.63(2H,q,J = 7.6Hz), 3.78(2H,s), 4.02(2H,s), 5.36(2H.s), 6.56(1H,s), 7.67(1H,s), 7.71(1H,d,J = 7.3Hz), 8.03(1H,dd,J = 6.6,5.9Hz), 8.09(1H,d,J = 6.6Hz),	
211	(solvent:$CDCl_3$/MeOD(4/1)) 1.26(3H,t,J = 7.6Hz), 1.29(3H,t,J = 7.3Hz), 2.59(3H,s), 2.69(2H,q,J = 7.5Hz), 3.68(2H,s), 4.05(2H,s), 4.20(2H,q,J = 7.3Hz), 5.29(2H,s), 6.46(1H,s), 7.52(1H,s), 7.67(1H,d,J = 7.9Hz), 7.95(1H,dd,J = 7.6,7.9Hz), 8.11(1H,d,J = 7.6Hz)	
212	(solvent:DMSO-d_6) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.50(1H,m), 3.78(1H,m), 4.74(1H,m), 5.30(2H,s), 5.46(1H,d,J = 2.0Hz), 6.49(1H,s), 6.69(1H,m), 6.85(1H,d,J = 7.9Hz), 6.91(1H,s), 7.13(1H,t,J = 7.9Hz), 7.56(1H,s), 7.67(1H,d,J = 7.6Hz), 7.98(1H,t,J = 7.6Hz), 8.08(1H,d,J = 7.6Hz), 8.51(1H,m), 9.08(1H,s), 12.61(1H,s)	
213	(solvent:DMSO-d_6) 1.19(3H,t,J = 7.6Hz), 2.58(3H,s), 2.64(2H,q,J = 7.6Hz), 3.85(2H,m), 4.55(1H,m), 5.34(1H,br), 5.39(2H,s), 6.60(1H,s), 7.68(1H,s), 7.74(1H,d,J = 7.6Hz), 8.05(1H,t,J = 7.6Hz), 8.12(1H,d,J = 7.6Hz), 8.63(1H,d,J = 8.3Hz), 12.55(1H,s), 12.90(1H,br)	

Table 140

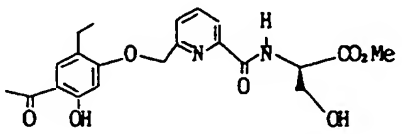
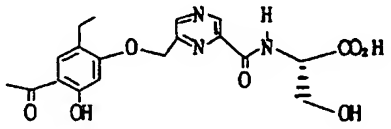
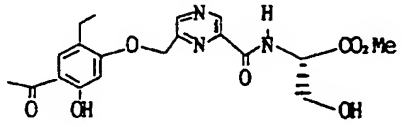
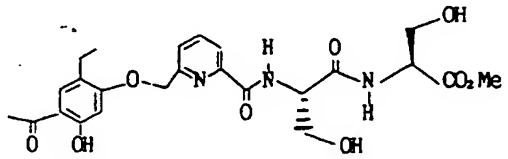
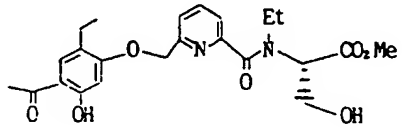
Ex. No.	Structural formula
214	
215	
216	
217	
218	

Table 141

	^{1}H-NMR δppm
214	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.58(3H,s), 2.68(2H,q,J = 7.6Hz), 3.85(3H,s), 4.11(2H,m), 4.88(1H,m), 5.29(2H,s), 6.52(1H,s), 7.49(1H,s), 7.65(1H,d,J = 8.3Hz), 7.91(1H,t,J = 8.3Hz), 8.15(1H,d,J = 8.3Hz), 8.80(1H,d,J = 8.3Hz) 12.69(1H,s)
215	(solvent:DMSO-d_6) 1.18(3H,t,J = 7.3Hz), 2.51(3H,s), 2.63(2H,q,J = 7.3Hz), 3.79(1H,dd,J = 11.2Hz,3.9Hz), 3.91(1H,dd,J = 11.2Hz,3.9Hz), 4.55(1H,m), 5.48(2H,s), 6.68(1H,s), 7.70(1H,s), 8.58(1H,d,J = 7.9Hz), 9.05(1H,s), 9.21(1H,s), 12.57(1H,s)
216	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.3Hz), 2.59(3H,br), 2.89(3H,s), 2.68(2H,q,J = 7.3Hz), 3.85(3H,s), 4.06(1H,dd,J = 11.2Hz,3.6Hz), 4.18(1H,dd,J = 11.2Hz,3.6Hz), 4.90(1H,m), 5.34(2H,s), 6.52(1H,s), 7.51(1H,s), 8.58(1H,m), 9.00(1H,s), 9.37(1H,s), 12.71(1H,s),
217	(solvent:$CDCl_3$) 1.27(3H,t,J = 7.6Hz), 2.60(3H,s), 2.71(2H,q,J = 7.6Hz), 3.79(2H,s), 3.85-4.10(4H,m), 4.64-4.80(2H,m), 5.33(2H,s), 6.49(1H,s), 7.57(1H,s), 7.72(1H,d,J = 7.6Hz), 8.00(1H,t,J = 7.6Hz), 8.10(1H,d,J = 7.6Hz)
218	(solvent:$CDCl_3$) 1.25(3H,t,J = 7.6Hz), 2.57(3H,s), 2.67(2H,q,J = 7.6Hz), 3.2-3.7(2H,m), 3.70(s,1.2H), 3.81(s,1.8H), 4.0-4.3(2H,m), 4.37(0.6H,m), 4.90(0.4H,m), 5.24(2H,s), 6.44(1H,s), 7.48(1H,s), 7.5-7.9(3H,m), 12.63(1H,s)

Table 142

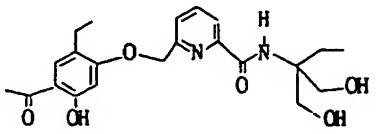
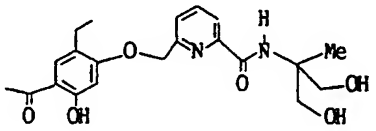
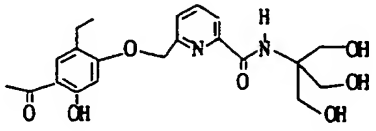
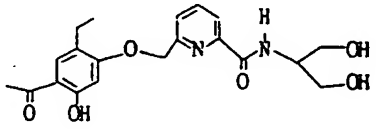
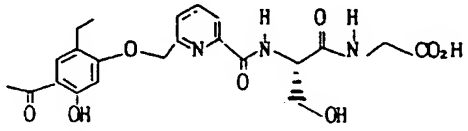
Ex. No.	Structural formula
219	
220	
221	
222	
223	

Table 143

	^{1}H-NMR	δppm
219	(solvent:$CDCl_3$) 1.00(3H,t,J=7.6Hz), 1.24(3H,t,J=7.6Hz), 1.81(2H,q,J=7.6Hz), 2.58(3H,s), 2.67(2H,q,J=7.6Hz), 3.72(2H,m), 3.94-4.06(4H,m), 5.27(2H,s), 6.56(1H,s), 7.48(1H,s), 7.63(1H,d,J=7.6Hz), 7.93(1H,t,J=7.6Hz), 8.15(1H,d,J=7.6Hz), 8.52(1H,brs), 12.73(1H,s),	
220	(solvent:$CDCl_3$) 1.24(3H,t,J=7.3Hz), 1.38(3H,s), 2.58(3H,s), 2.67(2H,q,J=7.3Hz), 3.7-4.1(6H,m), 5.27(2H,s), 6.56(1H,s), 7.48(1H,s), 7.64(1H,d,J=7.6Hz), 7.92(1H,t,J=7.6Hz), 8.14(1H,d,J=7.6Hz), 8.49(1H,s), 12.73(1H,s)	
221	(solvent:$CDCl_3$) 1.22(3H,t,J=7.6Hz), 2.57(3H,s), 2.65(2H,q,J=7.6Hz), 3.83(8H,s), 5.29(2H,s), 6.66(1H,s), 7.46(1H,s), 7.65(1H,d,J=6.6Hz), 7.93(1H,t,J=7.6Hz), 8.14(1H,d,J=7.9Hz), 9.12(1H,s), 12.82(1H,s)	
222	(solvent:$CDCl_3$) 1.26(3H,t,J=7.6Hz), 2.58(3H,s), 2.67-2.72(2H,m), 3.75-3.82(2H,m), 3.83-3.95(2H,m), 4.14-4.20(1H,m), 4.20-4.26(2H,m), 5.27(2H,s), 6.45(1H,s), 7.50(1H,s), 7.62(1H,d,J=6.9Hz), 7.92(1H,t,J=6.9Hz), 8.13(1H,d,J=6.9Hz), 8.53(1H,d,J=7.9Hz), 12.66(1H,s)	
223	(solvent:DMSO-d_6) 1.21(3H,t,J=7.6Hz), 2.58(3H,s), 2.65(2H,q,J=7.6Hz), 3.7-3.9(4H,m), 4.61(1H,m), 5.05(1H,br), 5.37(2H,s), 6.58(1H,s), 7.65(1H,s), 7.71(1H,dd,J=6.8Hz,2.1Hz), 8.02-8.25(2H,m), 8.39(1H,t,J=5.8Hz), 8.62(1H,d,J=8.3Hz), 12.54(1H,s),	

Table 144

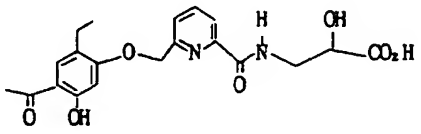
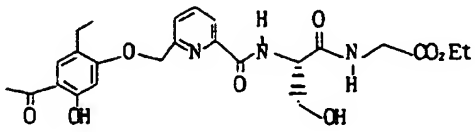
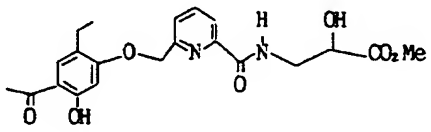
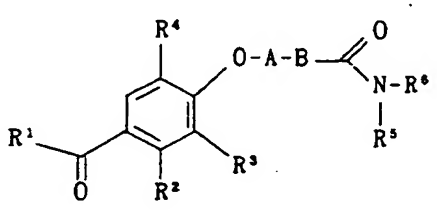
Ex. No.	Structural formula
224	
225	
226	

Table 145

	^{1}H-NMR	δppm
224	(solvent:DMSO-d_6) 1.21(3H,t,J=7.6Hz), 2.57(3H,s), 2.64(2H,q,J=7.6Hz), 3.54(1H,m), 3.72(1H,m), 4.19(1H,m), 5.34(2H,s), 5.59(1H,br), 6.55(1H,s), 7.63(1H,s), 7.69(1H,dd,J=6.1Hz,2.8Hz), 8.05(2H,m), 8.51(1H,t,J=6.1Hz), 12.55(1H,s), 12.65(1H,br)	
225	(solvent:$CDCl_3$) 1.25(3H,t,J=7.6Hz), 1.26(3H,t,J=7.3Hz), 2.58(3H,s), 2.68(2H,q,J=7.6Hz), 3.10(1H,dd,J=8.9Hz,5.6Hz), 3.80-3.88(1H,m), 4.06(2H,d,J=5.6Hz), 4.20(2H,qJ=7.3Hz), 4.25.4.35(1H,m), 4.70(1H,m), 5.28(2H,s), 6.45(1H,s), 7.15(1H,br), 7.49(1H,s), 7.63(1H,d,J=6.9Hz), 7.92(1H,t,J=6.9Hz), 8.15(1H.d,J=6.9Hz), 8.85(1H,d,J=7.6Hz), 12.66(1H,s)	
226	(solvent:$CDCl_3$) 1.25(3H,t,J=7.6Hz), 2.58(3H,s), 2.68(2H,q,J=7.6Hz), 3.57(1H,d,J=5.3Hz), 3.83(3H,s), 3.88(2H,m), 4.44(1H,m), 5.25(2H,s), 6.47(1H,s), 7.49(1H,s), 7.63(1H,d,J=7.6Hz), 7.91(1H,t,J=7.6Hz), 8.14(1H,d,J=7.6Hz), 8.36(1H,br), 12.68(1H,s)	

Claims

1. A compound represented by the formula :



wherein

A is a C_1-C_5 alkylene chain;

B is a phenylene or 6 membered heteroaromatic group which is constituted by carbon atoms and one or two nitrogen atoms, and B may be, optionally substituted with one or two substituents selected from the group, consisting of a C_1-C_5 alkyl group, a C_1-C_5 alkoxy group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

R^1 is a C_1-C_5 alkyl group;

R^2 is a hydroxyl group or a C_1-C_5 alkoxy group;

R^3 and R^4 are each independently a hydrogen atom, a C_1-C_5 alkyl group, a C_2-C_5 alkenyl group or a C_2-C_5 alkynyl group;

R^5 is a hydrogen atom, a C_1-C_5 alkyl group or a hydroxy C_1-C_5 alkyl group;

R^6 is a group of the formula:

-X-Y-Z-$R^{6'}$

wherein X is a phenylene group or a monocyclic 5~ 6 membered hetero aromatic group, and X is optionally substituted with one or two substituents selected from the group consisting of a C_1-C_5 alkyl group, a hydroxyl group, a carboxyl group, a nitro group and a halogen atom;

Y is a single bond or an oxygen atom;

Z is a single bond or a C_1-C_5 alkylene chain;

provided that when Y is an oxygen atom,

X is a phenylene group and Z is a C_1-C_5 alkylene chain;

$R^{6'}$ is a $COOR^7$ group,

a $CONR^8R^9$ group,

a $CONHCHR^{20}(CH_2)_nCOOR^7$ group,

a $CONHCHR^{20}(CH_2)_nCONR^8R^9$ group,

a $CONHCHR^{20}CONHCHR^{22}CO_2R^7$ group or

a sulfamoyl group,

wherein R^7 is a hydrogen atom, a benzyl group, a C_1-C_5 alkyl group or an C_1-C_5 alkyl group substituted with an aminoheteroaromatic group wherein the heteroaromatic group is a monocyclic 5–6 membered heteroaromatic group;

R^8 and R^9 are each independently a hydrogen atom, a C_1-C_5 alkyl group, hydroxy C_1-C_5 alkyl group, a hydroxyethylpyridyl group or a hydroxyethylthiazolyl group, or the group of the formula:

$-NR^8R^9$

represents a pyrrolidino, a piperidino or a morpholino group;

R^{20} is a hydrogen atom, a hydroxyl group, a C_1-C_5 alkyl group, a phenyl group, a hydroxyphenyl group, a benzyl group, a hydroxy benzyl group or a substituted C_1-C_5 alkyl group wherein the substituent is selected from the group consisting of a hydroxyl group, a C_1-C_5 alkoxy group, a mercapto group, a methylthio group, an amino group, an indolyl group, an imidazolyl group, a carboxyl group, a C_1-C_5 alkoxycarbonyl group, a carbamoyl group and a guanidino group;

n is 0, 1, 2, 3, 4 or 5; and

R^{22} is a hydrogen atom, a C_1-C_5 alkyl group or a C_1-C_5 hydroxyalkyl group;

or R^5 is a $CHR^{20}(CH_2)_nCOOR^7$ group,

a $CH_2CHR^{20}COOR^7$ group,

a $CHR^{20}(CH_2)_nCONR^8R^9$ group,

a $CH_2CHR^{20}CONR^8R^9$ group,

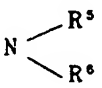
a $CHR^{20}(CH_2)_nOH$ group,

a $CR^{20}R^{22}(CH_2)_nOH$ group,

a $CH_2CHR^{20}OH$ group, or

a $CHR^{20}CONHCHR^{22}CO_2R^7$ group,

wherein R^7, R^8, R^9, R^{20}, R^{22} and n are as defined above, or the group of the formula:



represents an azetidino group, pyrrolidino group, a piperidino group or a homopiperidino group, which is optionally substituted with one to two substituents selected from the group consisting of a hydroxyl group, a C_1-C_5 hydroxyalkyl group, carboxyl group, C_1-C_5 alkoxycarbonyl group and benzyloxycarbonyl group; or pharmaceutically acceptable salts thereof.

2. The compound according to claim 1, wherein R^1 is a methyl group and R^2 is a hydroxyl group.

3. The compound according to claim 1, wherein R^3 is a hydrogen atom and A is a methylene group.

4. The compound according to claim 1, wherein R^1 is a methyl group, R^2 is a hydroxyl group, R^3 is a hydrogen atom and A is a methylene group.

5. The compound according to claim 4, wherein B is a 2,6-pyridinediyl, a 2,4-pyrimidinediyl or a 2,6-pyridinediyl N-oxide group.

6. The compound according to claim 4, wherein R^6 is a group of the formula:

$X\text{-}Y\text{-}Z\text{-}R^{6'}$

(wherein X, Y, Z and $R^{6'}$ are as defined in claim 1).

7. The compound according to claim 4, wherein R^6 is a group of the formula:

$CHR^{20}(CH_2)_nCOOR^7$

(wherein R^{20}, R^7 and n are as defined in claim 1).

8. The compound according to claim 4, wherein R^6 is a group of the formula:

$CHR^{20}(CH_2)_nCONR^8R^9$

(wherein R^{20}, R^8, R^9 and n are as defined in claim 1).

9. The compound according to claim 4, wherein R^6 is a group of the formula:

$CHR^{20}CONHCHR^{22}CO_2R^7$

(wherein R^{20}, R^{22}, R^7 and n are as defined in claim 1).

10. The compound according to claim 4, wherein R^4 is an ethyl group.

11. The compound according to claim 5, wherein X is a 2,6-pyridinediyl group.

12. The compound according to claim 10, wherein $R^{6'}$ is a group of the formula:

$COOR^7$

(wherein R^7 is as defined in claim 1).

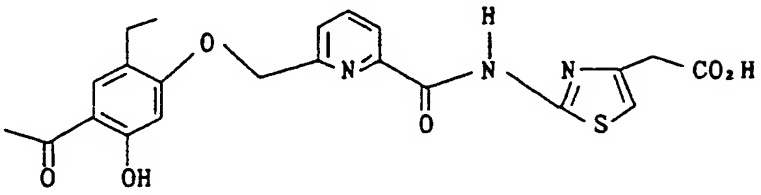
13. The compound according to claim 13, wherein $R^{5'}$ is a carboxyl group.

14. The compound according to claim 10, wherein $R^{6'}$ is a group of the formula:

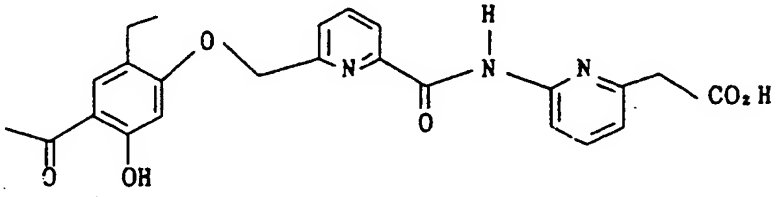
$CONHCHR^{20}(CH_2)_nCOOR^7$

(wherein R^{20}, R^7 and n are as defined in claim 1).

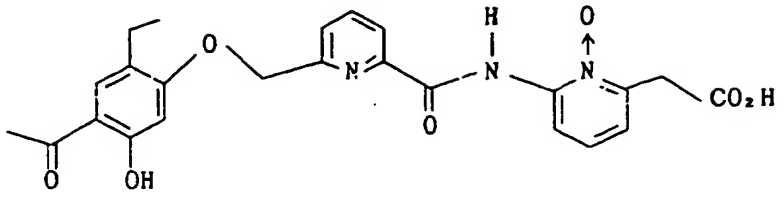
15. A compound of the formula:



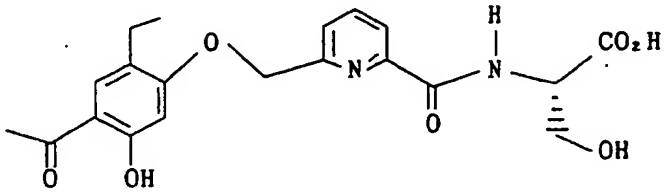
16. A compound of the formula:



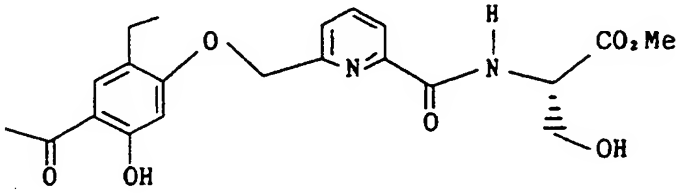
17. A compound of the formula:



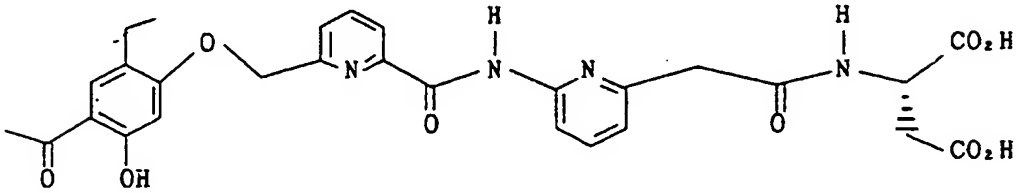
18. A compound of the formula:



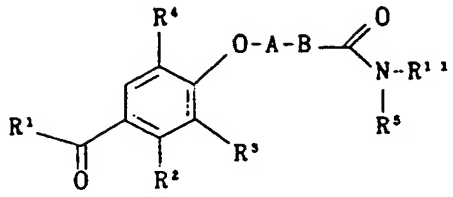
19. A compound of the formula:



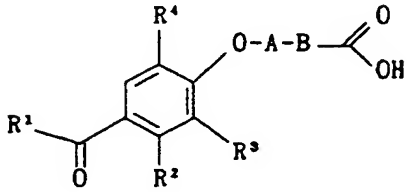
20. A compound of the formula:



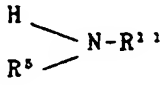
21. A process for producing a compound as claimed in claim 1 which comprises:
(a) to produce a compound of the formula:



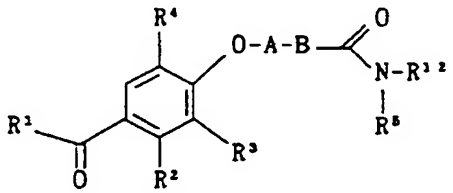
reacting a compound of the formula:



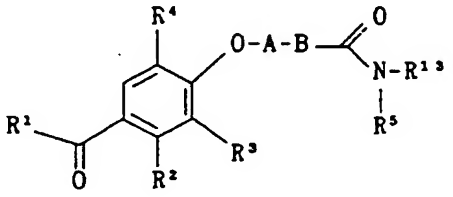
with a compound of the formula:



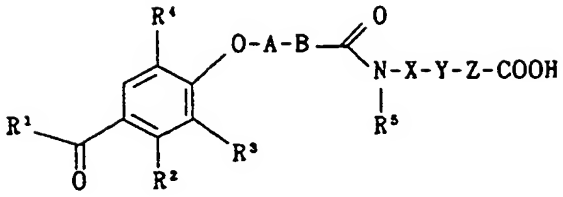
(b) hydrolyzing a compound of the formula:



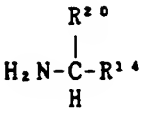
to produce a compound of the formula:



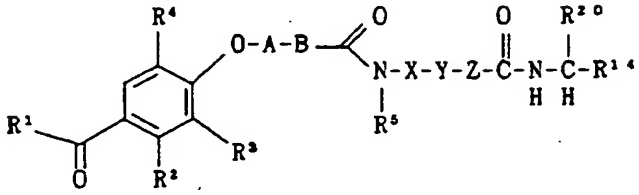
(c) reacting a compound of the formula:



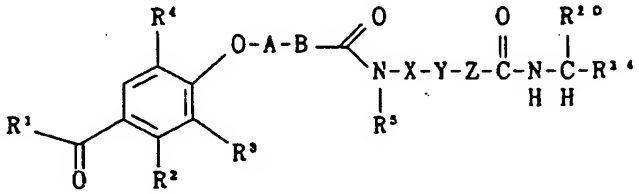
with a compound of the formula:



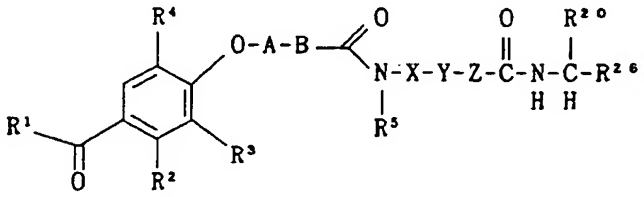
to produce a compound of the formula:



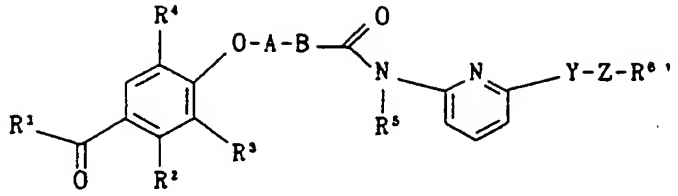
(d) hydrolyzing a compound of the formula:



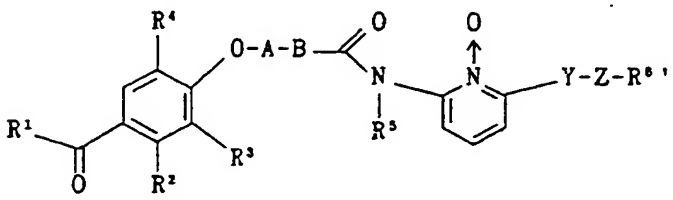
to produce a compound of the formula:



(e) oxidizing a compound of the formula:

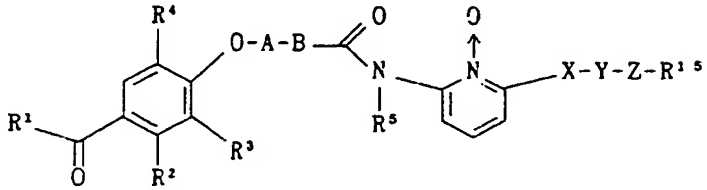


to produce a compound of the formula:

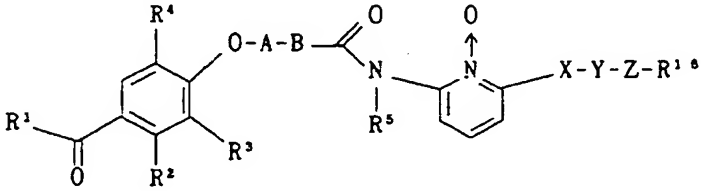


or

(f) hydrolyzing a compound of the formula.



to produce a compound of the formula:



wherein R^1, R^2, R^3, R^4, R^5, $R^{6'}$, R^{20}, A, B, X, Y and Z are as defined in claim 1,

R^{11} is the same as $R^{5'}$, but it does not mean free carboxylic group;

R^{12} is a group of the formula:

$X\text{-}Y\text{-}Z\text{-}COOR^{7'}$,
$X\text{-}Y\text{-}Z\text{-}CONHCHR^{20}(CH_2)_n\ COOR^{7'}$,
$X\text{-}Y\text{-}Z\text{-}CONHCHR^{20}CONHCHR^{22}CO_2R^{7'}$,
$CHR^{20}(CH_2)_nCOOR^{7'}$,
$CH_2CHR^{20}COOR^{7'}$, or
$CHR^{20}CONHCHR^{22}COOR^{7'}$,

wherein X, Y, Z, R^{20}, R^{22} and n are as defined above, and $R^{7'}$ is the same as R^7 but it does not mean a hydrogen atom,

R^{13} is a group of the formula:

X-Y-Z-COOH,
X-Y-Z-CONHCHR^{20}(CH$_2$)$_n$ COOH,
X-Y-Z-CONHCHR^{20}CONHCHR^{22}CO$_2$H,
CHR^{20}(CH$_2$)$_n$COOH,
CH$_2$CHR^{20}COOH, or
CHR^{20}CONHCHR^{22}COOH,

wherein X, Y, Z, R^{20}, R^{22} and n are as defined above.

R^{14} is a group of the formula:

(CH$_2$)$_n$COOR$^{7'}$, or
CONHCHR^{22}COOR$^{7'}$,

wherein $R^{7'}$, R^{22} and n are as defined above.

R^{15} is a group of the formula:

COOR$^{7'}$,
CONHCHR^{20}(CH$_2$)$_n$COOR$^{7'}$, or
CONHCHR^{20}CONHCHR^{22}CO$_2$R$^{7'}$,

wherein $R^{7'}$, R^{20}, R^{22} and n are as defined above.

R^{16} is a group of the formula:

COOH,
CONHCHR^{20}(CH$_2$)$_n$COOH, or
CONHCHR^{20}CONHCHR^{22}CO$_2$H,

wherein R^{20}, R^{22} and n are as defined above.

R^{26} is a group of the formula:

(CH$_2$)$_n$COOH, or
CONHCHR^{22}COOH,

wherein R^{22} and n are as defined above.

22. A pharmaceutical composition useful as an antiinflammatory agent or an antiallergic agent, which comprises an effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof as an active ingredient and a pharmaceutiacally acceptable carrier or diluent.

23. A method of treating inflammatory or allergic states which comprises administering a pharmaceutically effective amount of a compound of claim 1 or a pharmaceutically acceptable salt thereof to a patient.

24. A compound of claim 1 for use as a medicament as an active therapeutic substance.

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

which under Rule 45 of the European Patent Convention shall be considered, for the purposes of subsequent proceedings, as the European search report

Application Number EP 92 10 8916

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	US-A-4 672 066 (M. CARSON et al.) * Claims 1-4,6,15,16,30; examples 31-38 * ---	1-5,22, 24	C 07 D 213/81 C 07 D 277/46 C 07 D 401/06 C 07 D 401/12 C 07 D 401/14 C 07 D 417/12 C 07 D 417/14 C 07 D 241/24 C 07 C 233/82 A 61 K 31/44 A 61 K 31/425
Y	CHEMICAL ABSTRACTS, vol. 111, no. 11, 11th September 1989, page 729, abstract no. 97094e, Columbus, Ohio, US; & JP-A-01 29 363 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD) 31-01-1989 * Abstract * ---	1-5,22, 24	
X	* CAS RN 122151-73-9 * ---	1-5,22, 24	
A	CHEMICAL ABSTRACTS, vol. 112, no. 3, 15th January 1990, page 494, abstract no. 20906j, Columbus, Ohio, US; & JP-A-01 104 052 (YOSHITOMI PHARMACEUTICAL INDUSTRIES, LTD) 21-04-1989 * Abstract * --- -/-	1-22,24	

TECHNICAL FIELDS SEARCHED (Int. Cl.5)

C 07 D
C 07 C
A 61 K

INCOMPLETE SEARCH

The Search Division considers that the present European patent application does not comply with the provisions of the European Patent Convention to such an extent that it is not possible to carry out a meaningful search into the state of the art on the basis of some of the claims

Claims searched completely :

Claims searched incompletely :

Claims not searched :

Reason for the limitation of the search:

Remark: Although claim 23 is directed to a method of treatment of (diagnostic method practised on) the human/animal body (Art. 52(4) EPC) the search has been carried out and based on the alleged effects of the compound/composition.

Place of search	Date of completion of the search	Examiner
THE HAGUE	01-09-1992	BOSMA P.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P0407)

European Patent Office

PARTIAL EUROPEAN SEARCH REPORT

Application Number EP 92 10 8916

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl. 5)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
A,D	EP-A-0 276 065 (ELI LILLY AND CO.) * Claims 1-7; examples * ---	1-20,22 ,24	
A	EP-A-0 174 770 (MERCK FROSST CANADA INC.) * Whole document * -----	1-22,24	
			TECHNICAL FIELDS SEARCHED (Int. Cl.5)

EPO FORM 1503 03.82 (P0410)

(19) Eur päisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 516 069 A1**

(12) EUROPEAN PATENT APPLICATION

(21) Application number: **92108916.5**

(22) Date of filing: **27.05.92**

(51) Int. Cl.5: **C07D 213/81**, C07D 277/46, C07D 401/06, C07D 401/12, C07D 401/14, C07D 417/12, C07D 417/14, C07D 241/24, C07C 233/82, A61K 31/44, A61K 31/425

(30) Priority: **31.05.91 JP 157725/91**

(43) Date of publication of application: **02.12.92 Bulletin 92/49**

(84) Designated Contracting States: **AT BE CH DE DK ES FR GB GR IT LI NL PT SE**

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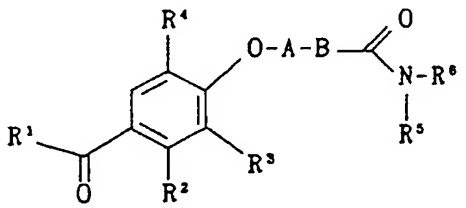
(74) Representative: **von Kreisler, Alek, Dipl.-Chem. et al**
Patentanwälte Von Kreisler-Selting-Werner,
Delchmannhaus am Hauptbahnhof
W-5000 Köln 1(DE)

(54) Leukotriene B4 antagonist.

(57) Leukotriene B_4 antagonists of the formula:



wherein each symbol is as defined in the specification, processes for producing them, and pharmaceutical compositions containing them. The compounds of the present invention are very useful as the drugs for the treatment of allergic and inflammatory diseases.

EP 0 516 069 A1

pfs no=91157725 cc=JP ls

NO : 91 157725 CC : JP

FAMILY MEMBERS

CC	PUBDAT	KD	DOC.NO.	CC	PR.DAT	YY	PR.NO.
				JP	1991/05/31	91	157725
AT	1996/05/15	E	137223				
AU	1993/03/11	A1	1719392				
AU	1993/11/04	B2	643140				
CA	1992/12/01	AA	2069667				
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GR	1996/08/31	T3	3020050				
JP	1993/09/17	A2	5239004				
MX	1993/01/20	A1	9202612				
US	1993/07/06	A	5225422				